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# Archives of Neurology and Psychiatry

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## INJURY OF THE CENTRAL NERVOUS SYSTEM RESULTING FROM DECOMPRESSION TO SIMULATED HIGH ALTITUDES

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**A**LTHOUGH the effects of decompression sickness as observed in caisson disease have been well known for many years, interest in this problem has recently been revived in connection with development of the same illness in aviators on ascent to high altitudes. Opportunity for studying this condition was provided during the training of approximately 470,000 airmen for flight to high altitude. In only 6 of this very large number of men did reactions or conditions develop directly or incidentally related to this training which resulted in fatalities. In the course of this training, trainees undergo a simulated "flight" in a decompression chamber. The pressure in this chamber is reduced in order to simulate high altitude, and the subject is instructed in the use of his equipment under these conditions.<sup>1</sup> If severe symptoms of decompression sickness develop, the subject is immediately returned to ground level for treatment and observation. In this respect, decompression sickness in aviators differs significantly from that developing in caisson workers. In the former, return to ground level is carried out promptly, permitting treatment of the subject in a normal environment. In caisson workers, symptoms develop after the victim returns to his normal environment, and treatment requires reexposure to an abnormal situation, from which he may be removed only slowly, frequently with recurrence of symptoms. Owing to these differences in environmental factors, there have been important differences in the types of trauma to which the person has been subjected. In the case of the caisson worker, the trauma may persist for some time before treatment (recompression) can be started. Furthermore, a study of the course of his disease may be obscured by the fact that if recompression and redecompression are not properly performed he may again be subjected to further trauma. The aviator, on the other hand, usually makes a prompt descent as soon as his symptoms become severe. Since he then remains on the

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1. Standard United States Army Air Forces "demand" oxygen equipment was used on these flights.

ground, there is no recurrence of trauma. As a result, it has become possible for the first time to observe the chain of events which follow a single bout of decompression sickness.

Study of the cases which have been observed in these circumstances reveals that symptoms tend to develop in two periods or phases. The first, or "primary," reaction occurs during decompression or immediately after return to normal atmospheric pressure. These symptoms are usually transitory and mild. The second, or "delayed," phase of the reaction develops from two to twelve hours after "descent," at a time when the subject may have appeared completely recovered from the early symptoms of his experience. The delayed symptoms are often persistent and severe. A given subject may show only a "primary" reaction or only a "delayed" reaction, or he may have both. The first phase often merges into the second phase, but the two phases are distinct and should be differentiated.

The following 3 cases illustrate the "primary" reaction to decompression.

#### REPORT OF CASES

CASE 1.—A 21 year old cadet was undertaking a rapid decompression to a simulated altitude of 38,000 feet (11,500 meters), followed by prompt recompression. Decompression was completed in ten minutes, and simulated descent was started immediately. At a simulated altitude of 35,000 feet (10,640 meters) the subject attempted to reach for an object with his right hand and suddenly discovered that he could not move his arm. He grasped the right hand with the left and raised it, but as soon as he let go it dropped back to his side. He realized that he had no sensation in the right side, as he had neither felt the right hand move nor had the sensation of the left hand grasping it. He then attempted to stand and found that the right leg was in the same condition. He told the chamber operator that he was weak. He did not appear confused. There was no evidence of shock. The rate of recompression was increased and within two minutes the chamber had reached a simulated altitude of 20,000 feet (6,080 meters). At this time, strength and sensation had begun to return. Five minutes later, on reaching "ground level," strength was apparently normal, and the subject was able to walk from the chamber without assistance.

Examination following the flight revealed questionable reduction of tendon reflexes in the right arm and leg. The Babinski sign was absent. There was no demonstrable sensory impairment. The cranial nerves were normal. The changes in reflexes could not be demonstrated an hour after the "flight." Except for slight lassitude, such as is frequently experienced after decompression, the subject evidenced no further symptoms.

CASE 2.—A 25 year old cadet remained at a simulated altitude of 33,000 feet (10,030 meters) for one hour and fifty-six minutes, at the end of which aching pain developed in the left knee and in each shoulder ("bends"). The pain became progressively worse, and four minutes later recompression of the chamber was started. With recompression, the subject experienced pain in the right ear (aer-otitus) and over the right eye (aerosinusitis). At a simulated altitude of 29,000 feet (8,800 meters) the joint pain was relieved. Shortly afterward, however, the subject became confused and dizzy. The faces of other men in the chamber became "blurred and run together," so that they could not be recognized. At about the

same time there developed numbness of the left hand. The subject thought his hand had "gone to sleep," although he had not been leaning on it. On reaching ground level, thirty minutes later, the subject walked from the chamber. He felt much improved, and his dizziness had disappeared. However, when he attempted to talk to the instructor, he found that he was unable to formulate any words. He responded to questioning by shaking his head to indicate that he could understand. He later described his condition by saying, "I knew what I wanted to say, and I knew I wasn't saying it; but I just couldn't bridge the gap." Examination at this time revealed mild aero-otitis of the right ear. There was no evidence of circulatory collapse. The blood pressure was 118 systolic and 92 diastolic; the pulse rate was 72 a minute. Sensory examination was not attempted. After resting about fifteen minutes, the subject started to read some charts on the wall and then discovered that his speech had returned. At the same time, the numbness of the left hand also disappeared.

During the next twelve hours the subject suffered from a severe right-sided headache, with nausea. He had no further symptoms.

Questioning revealed that he had had occasional unilateral headaches accompanied with scintillating scotomas. The last attack occurred about a year prior to the flight.

In attempting to explain a left hemianesthesia with aphasia, it should be noted that, although the subject was right handed, he had shaved with his left hand ever since forced to learn to do so on fracturing his right hand in 1939. His father and brother were ambidextrous.

CASE 3.—A flight surgeon aged 34 underwent slow decompression to a simulated altitude of 38,000 feet (11,500 meters) over a period of thirty-eight minutes. Ten minutes after reaching this altitude, he suddenly experienced severe pain in the left knee and, immediately thereafter, in the abdomen. He attempted to rise to go into the "lock" for recompression, but when he attempted to do so he collapsed. Recompression was begun immediately, and ground level was reached in three minutes. During this period the subject was pale and covered with perspiration. The pulse was extremely slow. He was semiconscious during descent. On reaching ground level, he attempted to rise but was too weak to do so. He complained that his right leg was weak and numb and that it felt as though cold water were flowing over it. He also complained of blurred vision. Gross examination revealed the presence of right homonymous hemianopsia.

Ten minutes after descent he had improved greatly. The pulse rate was 62 and the blood pressure 108 systolic and 72 diastolic. The visual symptoms had disappeared, and only a general feeling of weakness remained. The patient stayed in bed until the following day, when he attempted to resume his duties, but he found it difficult to concentrate on his work. However, at the end of forty-eight hours he was entirely recovered.

The following case is included with those of early reactions, although it differs from the other cases presented here in that it may represent a lesion of the spinal cord or a spinal nerve root rather than a cerebral lesion. It represents a type of disturbance frequently reported among caisson workers, but rare in cases of decompression to high altitude.

CASE 4.—A gunnery student aged 33 experienced pain in and numbness of the right forearm, spreading to the upper part of the arm and then to the left arm

after seventeen minutes at a simulated altitude of 38,000 feet (11,500 meters). He became faint and had paralysis of the right arm three minutes later. Recompression to ground level was begun immediately. There was no loss of consciousness. After descent he showed a moderate neurocirculatory reaction. The numbness and the flaccid paralysis of the right arm, with absence of tendon reflexes, persisted for over two hours and then gradually improved. There were no residual symptoms.

The outstanding features of the early reactions are their development during or immediately after the flight, their short duration and the focal character of the lesion. Symptoms observed include visual disturbances, aphasia, monoplegia, hemiplegia, hemianesthesia, confusion, amnesia and emotional disturbances.<sup>2</sup> Injury to the spinal cord and vestibular reactions, which are the commonest neurologic manifestations of caisson disease, are rare at high altitude. The commonest picture observed at high altitude is one which closely resembles an attack of migraine, and which occurs frequently, but not exclusively, in persons having a previous history of such episodes<sup>3</sup> (case 2).

The majority of subjects in whom such "primary" neurologic disturbances develop recover promptly and have no further difficulty. A few, however, had recurrence of symptoms, leading to the secondary, or "delayed," phase of the reaction. Other subjects exhibited delayed symptoms without ever having shown a "primary" phase. Although relatively uncommon, the secondary, delayed, reaction is a serious problem, since it is associated with extensive cerebral damage which may prove fatal. The following 3 fatal cases serve to illustrate the extent and severity of the late reaction.

CASE 5.—A student gunner aged 22 remained for nineteen minutes at a simulated altitude of 30,000 feet (9,120 meters). At the end of this time he complained that his left leg felt stiff. Shortly afterward he became nauseated and began to cough (symptoms of "chokes"). He appeared to become confused and then collapsed. Recompression to ground level pressure was begun within four minutes. During this period he remained unconscious and had violent stiffening of the back. The pulse was strong but at one time apparently stopped for about fifteen seconds.

He regained consciousness shortly after "descent," and when hospitalized five minutes later he appeared rational but slightly confused. He did not appear to be in shock. His blood pressure was 137 systolic and 80 diastolic, and the pulse rate was 88. No abnormal or pathologic reflexes were noted.

About two hours after descent he began to become restless and to evidence difficulty in speaking and in using his right arm. At the end of an hour he had become wildly delirious—entirely irrational, but responsive to the slightest stimulus. There was weakness of the right side of the face. The right arm was held rigid and in 90

2. Brown, G. A.; Cronick, C. H.; Motley, H.; Kocour, E. J., and Klingman, W. O.: Nervous System Dysfunction in Adaptation to High Altitude and as Post-flight Reactions, *War Med.* 7:157 (March) 1945.

3. Engel, G. L.; Webb, J. P.; Ferris, E. B., Jr.; Roman, J.; Ryder, H., and Blankenhorn, M. A.: A Migraine-Like Syndrome Complicating Decompression Sickness, *War Med.* 5:304 (May) 1944.

degree flexion. A Babinski sign was observed constantly on the right and inconsistently on the left.

During the ensuing eight hours there was continued violence, with deepening coma. There were evidences of shock (hemoconcentration, rapid pulse, pallor and sweating), for which intravenous injections of dextrose, isotonic solution of sodium chloride and plasma were administered. On the morning after the "flight" (twenty-four hours after descent), the patient still responded to stimuli but remained stuporous. The pupils were dilated and equal and reacted sluggishly to light. Examination of the ocular fundi revealed considerable blurring of the nasal margin of each disk, suggesting early papilledema. There was some weakness of the right side of the face, and the Babinski signs were elicited as before.

During the course of the day there was deepening coma. Pulmonary edema developed, and the temperature rose to 106.8 F. The patient died thirty-nine hours after being removed from the chamber.

Autopsy revealed intense pulmonary edema. The pericardium contained 75 cc. of clear fluid. The brain weighed 1,730 Gm. The exposed dura was tense throughout and showed extreme congestion. In the left parietal region, paramedially, a focus of dark blue discoloration, 2 by 1 cm., was noted. On close examination, the dura was observed to be lacerated,<sup>4</sup> and in this area the cerebral substance protruded through the opening. On exposure of the brain, a great accumulation of jelly-like translucent fluid was noted in the subarachnoid and perivascular spaces. The arachnoid was edematous and congested. The convolutions were greatly flattened and the sulci shallow. There were mild hemorrhages in the leptomeninges in the region of the parietal, occipital and frontal lobes. Each hemorrhage was about 1 cm. in diameter.

CASE 6.—A pilot aged 23 remained at a simulated altitude of 30,000 feet (9,120 meters), for twenty-one minutes, then became dizzy and began to cough. He broke out in a cold sweat and collapsed. The left pupil was widely dilated; the eyes were turned up and outward. The arms were stiff; the thumbs were flexed in the palm. Recompression to "ground level" pressure was reached within seven minutes after onset of symptoms.

He recovered sufficiently, shortly after descent, to respond to simple commands; but on admission to the hospital, forty minutes later, he was again unconscious and cyanotic. The blood pressure was 100 systolic and 30 diastolic; the pulse rate, 120, and the respiratory rate, 45. He did not move his left arm or leg. The tendon reflexes of the left arm and leg were exaggerated. The Babinski sign was present on the left.

The patient remained comatose and hemiplegic from this time until his death, fifty-six hours later. The course was marked by deepening stupor and accompanying shock. Three hours after descent he suddenly ceased breathing. Artificial respiration was initiated, after which shallow respiration was resumed. Eight hours after descent there was a sharp fall in blood pressure to a value of 90 systolic. The pulse rate was 150. Plasma was administered, and the blood pressure subsequently returned to 130 systolic and 80 diastolic but fell again prior to the patient's death. About thirty hours after descent there were observed tetanic twitchings of the left arm, leading at times to rather severe generalized convulsive movements of the whole body. Terminally, there were pronounced cyanosis, pulmonary congestion and rapid pulse.

Autopsy revealed 30 cc. of clear fluid in each pleural cavity and 20 cc. in the pericardial sac. There was intense pulmonary edema. Grossly, the brain weighed

4. The nature of the dural defect has not been definitely established.

1,424.5 Gm. The convolutions were slightly flattened. All the superficial blood vessels were slightly injected. Multiple sections from the cerebral cortex all showed degenerative changes in the nerve cells. There was moderate hyperemia but no evidence of hemorrhage.

CASE 7.—An aviation cadet aged 25 remained for ten minutes at a simulated altitude of 38,000 feet (11,500 meters). At the end of this time mild abdominal pain (gas pains) developed. This disappeared, but twenty-five minutes later he had steady, moderate pain in the right wrist ("bends"). Shortly afterward, he became pale and respiration became rapid and deep. The right arm hung limply at the side, although it is not certain whether this was due to pain or weakness. Recompression was begun, and the pressure reached "ground level" fifty-seven minutes after the start of the "flight." At this time his pain had disappeared, and the subject walked from the chamber. His general condition seemed satisfactory. The pulse rate was 60 and the blood pressure 100 systolic and 60 diastolic. Routine examination showed no indication that he was experiencing more than mild neurocirculatory disturbance after a case of the "bends."

The patient remained reclining for the next fifteen minutes. At the end of that time he began to sweat profusely. Shortly afterward he complained, for the first time, of weakness of the right hand. There were no other symptoms. Mentally he appeared entirely normal.

Two hours after descent he was observed to be somewhat drowsy but otherwise normal. One and one-half hours later, however, he was irrational and restless. During the afternoon, he became progressively more restless and stuporous, thrashing about with his left arm and leg, but being apparently unable to use the right side. He had ankle clonus on the right and a Babinski sign bilaterally. Seven hours after descent, the hematocrit reading was found to be elevated, and intravenous injections of saline solution and plasma were given. Eight hours after descent, he had a sudden circulatory collapse, and the temperature had risen to 107.6 F. Prompt administration of large amounts of fluid was followed by improvement in the circulation. Ice packs were applied, and the temperature was reduced. There was an unexplained obstruction of respiration fifteen hours after descent, relief for which was obtained only by tracheotomy.

After this severe crisis, the patient's general condition improved, and he lived seventy hours after the flight. Death apparently resulted from pulmonary edema. However, in spite of the general improvement, the neurologic signs at no time improved. The patient remained comatose and restless, with right hemiparesis, until the time of death. During the second day there were observed tetanic movements of the right side of the face, at times almost convulsive in character.

Autopsy revealed 30 cc. of fluid in the pericardial space. There was considerable pulmonary edema, with areas of pneumonic consolidation.

Examination of the fresh brain revealed moderate congestion of the meningeal vessels. The gyri appeared flatter and the sulci shallower than normal. After fixation in dilute solution of formaldehyde U.S.P., the brain was examined, and no abnormalities of the surface were noted. Sections through the pons and medulla revealed no hemorrhage or softening. Multiple cross sections of the cerebral hemispheres were made. Softening was observed in the region of the basal ganglia on each side; this appeared to be due to postmortem degeneration, resulting from inadequate fixation.

The following 2 cases illustrate the long interval that may intervene between the time of the "flight" and the appearance of neurologic symptoms. This interval varied from a few minutes to twelve

hours. In some instances the subject appeared free from symptoms during this period. In others there were general symptoms prior to the recurrence of neurologic disturbances.

CASE 8.—A gunnery student aged 32 remained at a simulated altitude of 38,000 feet (11,500 meters) for sixty-five minutes and then suddenly collapsed. He remained unconscious for twenty minutes after recompression and then apparently recovered. However, five hours after descent there developed weakness and then complete loss of motion of his right arm, accompanied with numbness. He was nauseated and vomited repeatedly. The following day the nausea subsided, and there was gradual return of strength and sensation. He felt entirely normal on the third day and showed no residual signs of his illness.

CASE 9.—A student pilot, aged 28, experienced pain in the left shoulder after thirty minutes at an altitude of 38,000 feet. Recompression was immediately begun, and he reached "ground level" ten minutes later. During the descent he became irrational but did not collapse. After resting for thirty minutes, he appeared entirely normal and was permitted to return to duty. However, six hours later he was admitted to the hospital, conscious, but weak, having collapsed while marching. At this time the pulse rate was 120 and the blood pressure 100 systolic and 80 diastolic. There was no evidence of neurologic injury. By the following morning he had become stuporous and restless and was observed not to use the left arm. Examination showed flaccid paralysis of the left arm, absence of the abdominal and cremasteric reflexes, absence of the deep reflexes in the left arm, weakness of the left side of the face, diminished pain sense in the left arm and confusion as to position of the toes. There was normal plantar flexion. Recovery was gradual but was complete within forty-eight hours. No residual symptoms were observed. Lumbar puncture, performed on the day after the flight, showed normal pressure, 3 cells per cubic millimeter and a negative reaction for globulin.

Convulsions were observed in the following 2 cases. In each case the subject was a carefully selected candidate for flying, with no previous history of a convulsive disorder. The convulsion was unquestionably an evidence of focal cerebral damage or of irritation in these cases.

CASE 10.—A student pilot aged 26 experienced pain in the right arm and in both knees after twenty-three minutes at an altitude of 38,000 feet (11,500 meters). During recompression, he collapsed and cold sweat, pallor, shallow respiration and urinary incontinence developed. He did not regain consciousness after "descent" but was restless, incontinent and irrational. Twenty-four hours later he was still comatose and restless. There was right hemiparesis. All the deep reflexes were hyperactive; the abdominal and cremasteric reflexes were absent. The arms and legs were semirigid. The left foot showed fanning of the toes on plantar stimulation. Lumbar puncture showed a pressure of 190 mm. of water, 31 cells per cubic millimeter and a Pandy reaction of 4 plus for globulin. Forty-eight hours after descent the patient had a series of right-sided jacksonian convulsions. A second lumbar puncture showed 115 cells per cubic millimeter (108 polymorphonuclear cells), a Pandy reaction of 4 plus and 84 mg. of sugar per hundred cubic centimeters. After this, the patient recovered gradually and was discharged, apparently free from symptoms, twenty-two days after his flight.

CASE 11.—A student pilot aged 22, while at an altitude of 30,000 feet (9,120 meters), suddenly experienced shaking of the arms and legs and noted difficulty in breathing and numbness of the right arm and leg. Profuse sweating developed.

Recompression was immediately begun. After descent, he seemed somewhat confused, but the numbness of the right side apparently cleared. On the day following descent he seemed improved but was still confused and restless. The second day after descent he suddenly had a generalized convulsion, after which he remained unconscious for two hours—cold, pale and sweaty, with dilated pupils. Lumbar puncture showed the spinal fluid to be under normal pressure. There were 4 cells per cubic millimeter and a trace of globulin (Pandy test). He made a gradual recovery after his convulsion and returned to duty a week later.

The essential features of the late reaction are its slow onset and diffuse character. Symptoms usually progress slowly over a period of two to twenty-four hours from a rather circumscribed paresis, or moderate intellectual impairment with confusion, to severe paralysis and deep coma. The symptoms remain at their peak for twenty-four to

*Summary of Examination of the Spinal Fluid*

Subject	Symptoms	Pressure	Cells, per Cu. Mm.	Reaction for Globulin (Pandy Test)	Sugar, Mg. per 100 Cc.
1 (case 11)	Confusion; anesthesia of right arm and leg; convulsion. Recovery in 60 hours	Normal	4	Trace	
2 (case 2)	Shock; headache; vomiting	Normal	1	Positive	78.5
3 (case 9)	Delirium; left hemiparesis. Recovery in 24 hours	Normal	3	Negative	
4 (case 10)	(a) Coma; right hemiparesis (b) After jacksonian seizures	190 mm. of water	31 115	++++ ++++	84
5	Coma; shock; weakness of left side of face; bilateral Babinski sign	4 mm. of Mercury	3 white cells; 28 red cells	++++	85
6*	Stupor; Babinski sign; hemiparesis	100 mm.		Protein 65 mg. 100 Cc.	

\*Case reported by Lund, D. W.; Lawrence, J. H., and Lawrence, L. B.; Case Reports on a Severe, Delayed Reaction with Cerebral Involvement Following Decompression, Project 396, Committee on Aviation Medicine, Dec. 15, 1944.

thirty hours; then, if recovery is to take place, they gradually regress. In fatal cases, death has occurred from thirty-nine to seventy hours after the onset of symptoms. The extent of the lesion is difficult to evaluate, since in the severe cases, deepening coma and severe shock make examinations unsatisfactory. However, there are frequently indications that both hemispheres are involved. Mental reactions have been peculiarly prominent. Confusion and irritability are frequent at the onset. Later, restlessness and delirium supervene, and in the final stages there is deep coma.

The most consistent laboratory finding has been leukocytosis, the count in severe cases ranging from 15,000 to 40,000 white blood cells

per cubic millimeter. In some cases hemoconcentration has also developed, but this has not been a constant finding in neurologic cases. Examinations of the spinal fluid (table 1) was carried out in 7 instances. In 1 case the spinal fluid was blood tinged. In case 10 in which hemiplegia was followed by a series of convulsions, lumbar puncture showed normal pressure of the spinal fluid, with a strongly positive reaction to the Pandy test. The cell count on the day prior to the convulsions was 31 per cubic millimeter, and on the day of the convulsions it was 115 per cubic millimeter (108 polymorphonuclear cells and 7 lymphocytes). In none of the fatal cases was a lumbar puncture performed.

There is a close relation between the delayed neurologic reaction and a condition of circulatory failure, or "shock," which it frequently accompanies. Like the delayed neurologic reaction, the circulatory disturbance also has a delayed and gradual onset. It is characterized by hemoconcentration and by pulmonary edema and pleural effusion. A severe circulatory reaction of this sort frequently occurs without there being any evidence of involvement of the nervous system, but severe neurologic disturbances rarely occur without an associated picture of shock. In the cases of neurologic involvement the cerebral damage may well be but one aspect of widespread injury to the body.

The mechanism leading to the development of neurologic reactions of the types described is obscure, but there is important evidence for a solution of this question. There is little doubt that they are in some way related to decompression, and probably to the evolution of gas from solutions within the body. Reactions of this sort are not seen after simple anoxia. They may occur in subjects who have not been anoxic while at high altitude. They take place only in association with flights to altitudes at which other symptoms of decompression sickness are common and at which gas bubbles within the tissues are known to be present.

The primary type of reaction appears to be closely associated with the actual presence of the bubbles within the body, as it is closely related with the symptoms of "bends" and "chokes." In caisson disease, it has been felt that symptoms resulted from bubbles forming within the parenchyma of the brain and spinal cord. It is difficult to explain the symptoms of the primary reaction on this basis. One can scarcely envisage a bubble forming within the brain tissue with such rapidity and to such a size as to produce hemianopsia or hemiparesis, yet producing such minor tissue injury that complete recovery might occur within fifteen minutes of recompression. Furthermore, this explanation can scarcely account for the development of symptoms during or after descent. Although bubbles are known to

persist in the body for periods up to four hours after descent,<sup>5</sup> one should expect tissue bubbles to produce their greatest disturbance at high altitude, when they are large, rather than after descent, when they have become small.

A more acceptable explanation of these symptoms is that they are due to intravascular bubbles producing cerebral air embolism. Animal studies<sup>6</sup>, in which cats were rapidly decompressed from a pressure of 5 atmospheres, have shown that after decompression the first site of appearance of bubbles in the exposed brain is within the arteries, and the course of events strongly suggests that many bubbles come to the brain through the systemic circulation, rather than actually forming in the brain itself. This explanation would account for the distribution of the lesions, their rapid onset and their prompt disappearance.

Two facts—the development of symptoms shortly after descent and their frequent occurrence in patients subject to migraine—point to a further element in the primary reaction, namely, vasospasm. It is possible that part of the damage which is produced by the lodgment of bubbles within the brain may be due to vasospasm. Spasm resulting from air embolism has been clearly demonstrated in mesenteric arteries.<sup>7</sup> There is less evidence that it occurs in the cerebral vessels. Villaret, Cachera and Fauvert<sup>18</sup> were able to demonstrate spasm of cerebral arteries after the intra-arterial injection of powdered pumice, but gas emboli did not produce spasm. Apparently, the degree of irritability of the vessel, as well as the severity of the stimulus, determines whether or not spasm will develop. The similarity of the symptoms observed in subjects with altitude decompression sickness to those seen in patients with migraine<sup>3</sup> and the frequency of neurologic symptoms at altitude in persons subject to migraine lend support to the belief that irritability of the cerebral vessels must play a part in the production of the primary type of reaction.

The occurrence of delayed reactions, such as those included in the second group of cases, indicates that with the disappearance of gas bubbles from the body further damage to the brain may still occur. An indication of how this damage may take place is to be found in the close association and similarity between the delayed neurologic

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7. Chase, W. H.: Anatomical and Experimental Observations on Air Embolism, *Surg., Gynec. & Obst.* **59**:569, 1934.

8. Villaret, M.; Cachera, R., and Fauvert, R.: L'embolie gazeuse cérébrale: Ses effets circulatoires locaux, *Compt. rend. soc. de biol.* **125**:108, 1937.

reaction and the delayed "shock" reaction which it frequently accompanies. It has been shown that a shocklike state, closely resembling that seen after decompression, can be produced in cats by the continuous intravenous injection of small bubbles of nitrogen.<sup>9</sup> This procedure damages the pulmonary capillaries, where the bubbles lodge, and leads to leakage of plasma from the capillaries, pulmonary edema and even pleural effusion. A gelatinous exudate is often seen in the region of the damaged vessels. It is likely that the delayed "shock" reaction is a similar process, resulting from the lodgment of gas bubbles within the lungs during flight. Other experimental evidence<sup>7</sup> indicates that a similar chain of events occurs in the mesenteric arteries after intra-arterial injection of bubbles. Here, there are observed, first, arteriospasm, followed by a hyperemic stage, which is characterized by edema and diapedesis of red cells. Aring<sup>10</sup> has described under the term "vasoparalysis" a similar reaction of the cerebral vessels following embolism. It is thus probable that the delayed neurologic reaction represents a form of cerebral edema, comparable to the pulmonary edema seen in the late "shock" reaction, and resulting from capillary and tissue injury caused by cerebral aeroembolism and vasospasm at the time of flight. The time course of the illness, its relation to the general "shock" reaction and the observation at autopsy of flattening of convolutions and gelatinous exudate, all lend support to this thesis.

#### SUMMARY AND CONCLUSIONS

During the course of altitude indoctrination of persons undergoing flight training in the Army Air Forces, a small number of neurologic reactions have been observed. The occurrence of these reactions in an altitude chamber provided an ideal opportunity for observing the chain of events which follows a bout of decompression sickness.

Neurologic reactions occurred in two phases—an early, or primary, reaction, appearing during or shortly after a flight, and a delayed, or secondary, reaction, occurring up to twelve hours after descent. Case reports of such reactions are presented.

The primary type of reaction is due to the lodgment of air bubbles within the cerebral vessels. It is possible that vasospasm resulting from the lodgment of the bubble may be an additional factor in the development of symptoms.

The delayed reaction is also vascular in origin and results from a change in permeability of the vascular wall secondary to its occlusion during the flight. On the disappearance of bubbles after des-

9. Hetherington, A. W., and Miller, R. A., School of Aviation Medicine, unpublished data.

10. Aring, C. D.: Vascular Diseases of the Nervous System, *Brain* **68**:28, 1945.

cent, the damaged vessels become dilated; the blood is stagnant, and the walls are permeable. Leakage of fluid results in cerebral edema and diffuse disturbance of cerebral function. At autopsy, flattening of the convolutions, a gelatinous exudate and, occasionally, small hemorrhages are noted.

The trauma which leads to the cerebral vascular reaction observed in these patients is an unusual one. However, the mode of reaction of the blood vessels is probably not unusual, and, as has been suggested by Aring,<sup>10</sup> may play a part in the development of symptoms in a number of other diseases of the brain.

The case material included in this report was obtained from the aviation physiologists, who carried on the altitude training program and handled the chamber reactions. In many instances, their case reports were used verbatim in this paper.

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## CLINICAL ASPECTS OF CEREBRAL CYSTICERCOSIS

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**S**TATISTICAL STUDIES indicate that the incidence of cerebral cysticercosis is high in Latin America. In Mexico, Robles<sup>1</sup> found that of a series of 100 cases of cerebral tumor 25 were of cysticercosis. Arana and Asenjo<sup>2</sup>, in Chile, found 25 cases of cysticercosis in a series of 202 cases of intracranial tumor.

It is the purpose of this paper to summarize the clinical experience of my colleagues and me with cerebral cysticercosis in Mexico. During five years of neurosurgical practice 17 cases were collected. The diagnosis was confirmed by operation or autopsy in 10 of the cases, and in the others it was made on clinical, roentgenologic and laboratory evidence. The literature has been extensively reviewed by Trelles and Lazarte<sup>3</sup>, Lopez Albo<sup>4</sup> and Dixon and Hargreaves<sup>5</sup>. The frequency of cerebral cysticercosis will undoubtedly increase in Great Britain and the United States in the years following the war because of the displacement of the great mass of the armed forces into infected areas.

### CLASSIFICATION OF CEREBRAL CYSTICERCOSIS

It is well known that cerebral cysticercosis produces a variable clinical picture. The factors responsible for this variability are the position, number, size and stage of development of the cysts. A further effect may be produced by secondary changes in the adjacent cerebral tissue and the leptomeninges, such as inflammation and infection. There is also the possibility of a toxic effect on the elements of the central nervous system.

In most cases there are multiple, diffuse cysts, although in a few instances solitary ones occur. The localization of the diffuse type can often be made by the predominance of symptoms pointing to one

1. Robles, C.: Consideraciones acerca de 100 casos de tumor cerebral operados, Mexico, 1944.

2. Arana, R., and Asenjo, A.: Ventriculographic Diagnosis of Cysticercosis of the Posterior Fossa, *J. Neurosurg.* **2**:181, 1945.

3. Trelles, J. O., and Lazarte, J.: Cisticercosis cerebral; estudio clinico, histopatológico y parasitológico, *Rev. neuro-psiquiat.* **3**:393, 1940.

4. Lopez Albo, W.: Aspectos clinicos de la cisticercosis del sistema nervioso central, Mexico, 1945.

5. Dixon, H. B. F., and Hargreaves, W. H.: Cysticercosis (*Taenia Solium*): A Further Ten Years' Clinical Study, Covering 284 Cases, *Quart. J. Med.* **13**:107, 1944.

area. The pure forms, however, are rare, and even in cases in which a predominance of symptoms is exhibited there may be many confusing signs. The course and evolution of the disease are also important and will be discussed later.

In this paper, cerebral cysticercosis is divided for clinical purposes into the following types:

1. Cortical cysticercosis
2. Ventricular cysticercosis
  - Isolated
  - Multiple
3. Basilar cysticercosis
  - (a) Predominantly in the region of the cisterna magna
  - (b) Predominantly in the cerebellopontile angle
  - (c) Predominantly in the anterior and middle cerebral fossae
4. Mixed, general and diffuse cysticercosis

*Cortical Cysticercosis.*—The cysts frequently occur on the surface of the cerebral cortex, and in the region of the motor area they may give rise to irritation, with resultant focal attacks or more generalized epileptic fits. The importance of cysticercosis as the cause of epilepsy in young persons, especially soldiers or ex-soldiers during or after service abroad, was emphasized in England by Sir William MacArthur.<sup>6</sup> In cases of cortical cysticercosis there are frequently other signs of dysfunction of either a motor or a sensory type or disturbances in speech or mental activities.

In most cases of cortical cysticercosis the lesions are multiple and are frequently combined with involvement of other organs, as will be mentioned later. The adjacent leptomeninges usually present an inflammatory picture, the so-called cortical arachnoiditis, which has been seen in surgical explorations. A single cyst may be located in the cortex. An example of this is seen in the case of a woman aged 44 with signs localized to the left motor area, as indicated by jacksonian attacks on the right side, followed by transient paresis of the right upper limb. Operation revealed an isolated cyst; this, however, did not exclude the possibility of asymptomatic cysts elsewhere.

*Ventricular Cysticercosis.*—Cysts in the ventricular system are the rarest form. They are most frequently observed in the fourth ventricle, more rarely in the lateral and third ventricles. Ventricular cysticercosis may be isolated or multiple.

The clinical picture of ventricular cysticercosis is that of increased intracranial pressure with hydrocephalus. Fairly typical features of these mobile cysts are the intermittence of the symptoms and the fact

6. MacArthur, W. P.: Cysticercosis as Seen in the British Army, with Special Reference to the Production of Epilepsy, *Tr. Roy. Soc. Trop. Med. & Hyg.* **27**:343, 1933.

that the headaches begin with, or are exaggerated by, postural changes.

We have seen a case, reported by Fuentes,<sup>7</sup> that of an 18 year old girl, with a history of headache, vomiting, diplopia, loss of vision, vertigo and disturbances of walking and standing of three years' duration. She also complained of peculiar attacks of headaches and vomiting associated with a vertiginous sensation, and at times during these attacks she would fall to the floor because of loss of power in the legs. She then appeared drowsy, and there was inability to speak or disturbance of consciousness with incoherent and difficult speech. These attacks might last up to twenty-four hours, and usually there was complete immobilization of the head in the same posture as that at the time the pain began. Neurologic examination showed bilateral papilledema, hypotonia of all the limbs and some ataxia. After an unsuccessful exploration of the cerebellum, the patient died, and autopsy showed an isolated and mobile cyst at the superior angle of the fourth ventricle, occluding the inferior outlet of the sylvian aqueduct. There were no other cysts elsewhere in the brain.

*Basilar Cysticercosis.*—One of the most frequent locations of cerebral cysts is in the leptomeninges and cisterns at the base of the brain. These basilar lesions are frequently associated with cortical or ventricular cysts; but, in spite of the tendency to multiplicity of lesions in this type, it is sometimes possible to recognize certain dominant signs and symptoms which aid in localization of the most important. With all these basilar lesions there is an associated arachnoiditis, which may have some effect in the production of the symptoms.

The cisterna magna is fairly commonly affected, and the following case illustrates the essential features:

CASE 1.—M. T. T., a woman aged 36, had a previous history of migraine-like headaches. There was no history of infection with tapeworm. For two years she had had headaches which radiated to the occipital region, occasionally accompanied with vomiting. For five months there had been attacks of vertigo, which were sometimes followed by loss of motor power. There had also been progressive loss of vision for one year.

Examination showed diminution of visual acuity, and the visual fields showed generalized constriction. There was blurring of both optic disks. On one occasion there was gross ataxia of the lower limbs and she was unable to stand or walk, whereas on another occasion, several days later, there were hardly any abnormal signs—only slight instability and deviation on walking. There were generalized hypotonia and some clumsiness in voluntary movements of both upper and lower limbs. The tendon jerks were brisk. Roentgenographic studies of the skull demonstrated erosion and destruction of the dorsum sellae and of the clinoid processes. There were small, diffuse calcifications within the skull.

The clinical picture of increased intracranial pressure and severe loss of vision, without great changes in the optic disks, and the presence of small, diffuse intracranial calcifications led to the diagnosis of cerebral cysticercosis. Ventriculographic

7. Fuentes, M.: Síndrome de obstrucción paroxística del agujero de Magendie, que denominamos "síndrome diencefalo-bulbar" en un caso de quiste único de cisticerco en el IV ventrículo, Arch. de neurol. y psiquiat. 4:217, 1942.

examination showed conspicuous dilation of both lateral ventricles, the third ventricle and the aqueduct. The cerebrospinal fluid gave positive complement reactions for cysticercosis and showed other characteristic changes. Exploration of the posterior fossa revealed intense arachnoiditis of the cisterna magna, which extended over the region of the vermis. A small cyst was observed in the cisterna magna.

In other cases of cysticercosis of the cisterna magna, the picture was somewhat similar, but in these cases, in addition to symptoms referable to the posterior fossa, there were indications of a more generalized spread of the disease, and these signs were considered of some importance in the diagnosis. The following case is an example:

CASE 2.—M. H. M., a woman aged 53, had a previous history of tenia in childhood. Twenty years prior to the present illness she had several convulsive attacks, preceded by a visual aura; these occurred at irregular intervals for four or five years and then stopped. During the past year she had complained of headaches, vertigo, loss of vision, instability and difficulty in walking.

Examination revealed bilateral papilledema, gross diminution of visual acuity, increased deep reflexes in both upper and lower limbs, pronounced tremor of the upper limbs and unsteadiness in walking, with a tendency to stagger to either side. The roentgenograms of the skull showed enlargement of the sella, but no calcification. Ventriculographic examination demonstrated conspicuous dilatation of the lateral and third ventricles. Studies of the cerebrospinal fluid revealed positive evidence of cysticercosis. Exploration of the posterior fossa disclosed intense arachnoiditis affecting the region of the cisterna magna and part of the cerebellum. When the arachnoid was opened, many vesicles were observed; these were removed from the cisterna magna and the lateral spaces between the medulla and the inferior portion of the cerebellum.

In this case, the long history of the initial convulsive attacks, twenty years before, and the recent signs and symptoms of increased intracranial pressure suggested the diagnosis of cerebral cysticercosis with local spread.

In case of basilar cysticercosis of the posterior fossa there is sometimes an extension into the cerebellopontile angle, with the clinical picture associated with a lesion in this area. Guevara Oropesa<sup>8</sup> reported a case of cysticercosis in which a diagnosis of acoustic neuroma was made because of increase of intracranial pressure, unilateral loss of hearing and caloric response, vertigo, nystagmus and an ataxic gait. Similar cases of cysticercosis have been observed in Mexico in which symptoms were referable to the cerebellopontile angle, such as involvement of the fifth and eighth cranial nerves and the cerebellum.

Other selective regions for basilar cysticercosis are the anterior and middle fossae. Cases of acute and subacute cysticercosis have been described, and these are associated with signs of meningeal irritation, fever and increased intracranial pressure. These symptoms are most

8. Guevara Oropesa, M.: Tumor del angulo pont-cerebeloso, *Arch. de neurol. y psiquiat.* 1:369, 1938.

commonly seen in small children (Robles<sup>9</sup>); but the commonest form of basilar cysticercosis in older subjects usually follows a slower course, and anatomically the cysts correspond to the so-called cysticercosis racemosa. When the process affects the anterior fossa, there are usually signs of involvement of the olfactory and optic nerves. Cysts in the middle fossa are usually associated with involvement of the oculomotor, trigeminal and facial nerves. There may also be symptoms and signs related to lesions of the diencephalon and the lower part of the frontal and temporal lobes. The basilar spread, however, is frequently diffuse, and the arachnoiditis extends over the entire base of the brain.

In the following case of cerebral cysticercosis, although there was evidence of involvement of a diffuse character, symptoms were related predominantly to the anterior and middle fossae and the base of the brain.

CASE 3.—J. D. I., a man aged 26, had no history of infection with tapeworm. For the past two and a half years he had complained of headaches, loss of memory and insomnia. He also had attacks during which he would fall and sometimes lose consciousness. Some of these attacks were preceded by an olfactory aura, and others were of a cataplexic type without loss of consciousness. In the past few months he had noticed gross diminution of vision. Examination revealed bilateral anosmia, secondary atrophy of the optic nerve with gross diminution of visual acuity, slight exophthalmos of the right eye, loss of the right corneal reflex, sensory disturbance over the right side of the face and tremor of the tongue. There was a conspicuous tremor of both upper and lower limbs. The knee jerk was increased on the left side, and the plantar response on that side was of extensor type. There had also been progressive and severe mental deterioration. The patient was practically blind, had been confined to bed for more than a year and showed intense and generalized hyperesthesia to all kinds of stimuli and to movement of any part of the body. The cerebrospinal fluid pressure, as measured during lumbar puncture, varied from 380 to 500 mm. of water. Roentgenograms of the skull showed multiple and diffuse erosions of the bone and several small, diffuse intracerebral areas of calcification. The sella was enlarged, and there was erosion of the dorsum, the floor and the posterior clinoid processes. Air studies showed hydrocephalus, with asymmetric dilatation of the lateral ventricles, the right ventricle being larger than the left. There was no filling of the third ventricle. Examination of the cerebrospinal fluid gave positive evidence of cysticercosis. Exploration of the left parietal region showed a small, sharp-edged area of erosion in the skull about 8 mm. in diameter; immediately beneath this area was a protrusion of the dura, and when it was opened a small vesicle appeared.

*Mixed, General or Diffuse Cysticercosis.*—In some cases of diffuse cysticercosis the clinical picture is complex. We have seen cases in which there was mental deterioration associated with lesions in the motor areas and the pyramidal tract, as well as involvement of the cerebellum and the cranial nerves. In the cases thus far described, al-

9. Robles, C.: Consideraciones acerca de la cisticercosis cerebral en los niños, Bol. med. hosp. inf. 2:193, 1945.

though the lesions were sometimes diffuse, there were signs and symptoms which localized at least some of the lesions with a fair degree of accuracy. The next case illustrates the confused picture which may occur in the cases of the diffuse type.

CASE 4.—M. I. P., a woman aged 40, had a history of convulsions for sixteen years. During the past five years she had experienced difficulty in walking, and there were changes in behavior as well as auditory and visual hallucinations. Examination revealed severe mental disturbances, such as disorientation, confusion, loss of memory, puerility, difficulty in comprehension and emotional changes. There was also some degree of motor apraxia. She had slight paresis of the right lower part of the face, some difficulty with voluntary movements of the right upper limb and increased tendon reflexes. There was slight ataxia of the upper limbs; the right lower limb was hypertonic, and the knee and ankle jerks were increased. She was unable to stand or walk, and there was gross ataxia of both lower limbs. The roentgenogram showed enlargement of the sella turcica with erosion of the dorsum and the posterior clinoid processes. There were a few small intracerebral areas of calcification. Both lateral ventricles and the third ventricle were moderately dilated. Examination of the cerebrospinal fluid gave positive evidence of cysticercosis. Autopsy revealed cysts in the cisterna magna. Intense arachnoiditis involved the basilar regions, and the ventricular system was greatly dilated. A single cyst was observed in the anterior portion of the right temporal horn.

It is interesting to note that in this case, as in 4 other cases of advanced generalized cysticercosis in this series, the mental changes were so severe that the patient had been in a psychiatric hospital for a number of years. In most of these cases the mental deterioration was associated with many neurologic signs and symptoms, such as epileptic fits, optic nerve atrophy, involvement of the cranial nerves, weakness, ataxia and tremor. In some cases, however, the mental symptoms dominated the picture, and there were no obvious neurologic abnormalities. Such cases raise the question whether the mental disorder is due to the cysticercosis or whether it represents a form of reaction in the particular patient. The psychosis in these cases is considered organic, and secondary to cysticercosis. In 1 case, although the diagnosis was not verified, there was a long history of over twenty years during which there were several periods of confusion and agitation. The clinical picture was that of a profound mental disorder, with disorientation, indifference, puerility, incoherent speech, emotional instability, negativism and delirious ideas of various types. Examination revealed no evidence of cysticercosis except for palpable subcutaneous nodules and a few intracranial calcifications at the base of the brain in the region of the third ventricle. Analysis of the cerebrospinal fluid gave positive evidence of cysticercosis on several occasions, and the encephalograms demonstrated enlargement of the lateral ventricles and advanced atrophy of the frontotemporal region of both hemispheres.

Another case in this group was that of a woman aged 24 who at the age of 3 years had sudden onset of transient paralysis and rigidity, which lasted for several

days and was followed by headache and vomiting. Seven years later she began to have epileptiform attacks, and six years after this transient left hemiplegia developed. In recent years she had had headaches, progressive loss of vision and organized visual hallucinations. On examination, she was found to be practically blind, with bilateral primary atrophy of the optic nerve. There were conjugate deviation of the head and eyes toward the right and pronounced difficulty in deviation of the eyes to the left and upward. There were also nystagmoid jerks to the left and diminished hearing in the left ear. The upper and lower limbs on the left side showed spastic weakness, with increased reflexes and ankle clonus; Hoffmann's sign was elicited on the left side, and plantar responses of extensor type were present bilaterally. There were tremor, ataxia, dysdiadokokinesis of both upper limbs and inability to stand. Vibratory and postural sense were diminished on the left side.

#### SYMPTOMS OF CEREBRAL CYSTICERCOSIS

Four main groups of symptoms are most commonly present in this condition and so deserve further elucidation. These are epileptiform attacks, signs of increased intracranial pressure, mental disturbances and loss of vision. The epileptiform phenomena are easily explained by the location of the cysts; they may be of general or focal type. There may also be an aura (olfactory, visual, or other type), according to the area affected. Increased intracranial pressure is associated with basilar and ventricular cysticercosis as a result of obstruction of the circulation of the cerebrospinal fluid by the cysts or of the secondary arachnoiditis.

Explanation of the mental and visual disturbances, however, is more difficult. Altered mental behavior appears especially in cases of generalized and diffuse types of cysticercosis. There is sometimes pronounced cortical atrophy, and, in my opinion, this is an influencing factor. Some authors have noted "toxic" and "diffuse" encephalitis in association with cysticercosis. It is impossible definitely to localize the cysts in cases in which mental changes are present; I believe, however, that, in addition to the diffuse involvement of the cortex, attention should be directed to the processes at the base of the brain, more specifically to the structures around the third ventricle, as was done in case 4. Visual disturbances are also prominent with the cerebral type of cysticercosis and may rapidly culminate in complete blindness, with secondary or primary atrophy of the optic nerve. The factors involved in this rapid development of visual deterioration are increased intracranial pressure, direct compression and invasion of the optic nerves by the cysts, or as a result of the secondary arachnoiditis, and possibly compression of the optic nerves by the dilated third ventricle, as a consequence of hydrocephalus. Besides these factors, there may be a toxic action on the optic nerves, although there is no positive evidence of this.

The presence of cysts in other parts of the body is an aid in the diagnosis of a cerebral lesion. We have seen intraocular cysts, and

it is important to make a careful examination of the entire body for cysts in the skin and subcutaneous tissues. In some of our cases histologic examination of a subcutaneous nodule confirmed the diagnosis. Cysts may also be disseminated in the muscles of the limbs, and if calcified they can easily be seen in a roentgenogram. Dixon and Hargreaves<sup>5</sup> recommended roentgenographic examination of the whole body, and in their series of 284 cases the roentgenographic study was by far the most important diagnostic method (with positive evidence in 212 cases). In many of the present cases there was no history of tapeworm infection, and Dixon and Hargreaves obtained a positive history of tenia in only 26 per cent of their cases.

#### DIFFERENTIAL DIAGNOSIS

The diagnosis of cerebral cysticercosis offers many difficulties because the disease may produce practically any neurologic picture. The diffuse and multiple character of the lesions is the cause of the amazing variety of neurologic symptoms, and even in those cases in which a predominance of symptoms points to an area of localization there are frequently many irrelevant symptoms.

The evolution and course of the disease are also of great importance. Sometimes the onset is sudden and acute, but frequently there is a history of many years' duration. Dixon and Hargreaves noted that the time between infection and the onset of cerebral symptoms is extremely variable, ranging from a few months to about twenty years. In small children, below 10 years of age, the course of the disease is frequently rapid, being sometimes associated with fever, headaches, convulsions, vomiting and other acute and generalized neurologic signs (Robles<sup>6</sup>). The course of the disease may be irregular, there being sometimes spontaneous remissions and long intervals between the appearances of the various symptoms, as in case 2, in which convulsive seizures preceded by twenty years the onset of increased intracranial pressure. Fairly characteristic of the condition is an irregular and diverse neurologic picture of a progressive nature, occurring generally in a young person, with a long history of variable symptoms. This slow, insidious and irregular course is an important feature in differentiating cysticercosis from tumors of the brain, although sometimes the diagnosis is difficult, especially in cases of the ventricular and cortical types. On the other hand, the progressive character and the presence of increased intracranial pressure in a great number of cases of cerebral cysticercosis serve to differentiate the disease from multiple sclerosis, and the remissions are not so complete and dramatic in the course of cysticercosis.

Neurosyphilis is a common possibility in the differential diagnosis of cysticercosis, especially of the diffuse type, in which there is no great increase in intracranial pressure and mental symptoms and signs of

cortical irritation are present. A careful analysis of the cerebrospinal fluid is of importance in the differentiation of cysticercosis and neurosyphilis, especially when there are no definite clinical or roentgenologic signs favoring the diagnosis of cysticercosis.

In some cases advanced cysticercosis may be diagnosed as cortical atrophy of the Pick or Alzheimer type. An example was the case of a woman aged 53 with epileptiform attacks and mental deterioration, but no increase in intracranial pressure. Encephalograms demonstrated dilatation of the ventricles and cortical atrophy, especially in the frontotemporal regions. The presence of small, diffuse intracranial calcifications and the results of analysis of the cerebrospinal fluid (great increase of cells with a large proportion of eosinophils, increase of albumin and globulin and positive reaction to the complement fixation test of cysticercosis) led to the correct diagnosis.

Another important point is the development of the cysticerci. In general the cysts have a tendency to die and become calcified; for this reason, some of the symptoms may disappear spontaneously for a time. This inactivity of the cysticerci is in contrast to other, possibly more active, states, in which they produce symptoms not only by their situation but by the severe meningeal reactions that frequently develop with the cysts. Dixon and Hargreaves expressed the belief that the natural function of the parasites is to remain alive in the tissues of their host and that when they die they swell and become tense with fluid, after which they shrink and become calcified. According to this concept, the cysticerci would produce more active symptoms immediately after death, and just before they become calcified.

#### VALUE OF ROENTGENOGRAPHIC STUDIES OF THE SKULL

The roentgenographic study of the skull is important in the diagnosis of cerebral cysticercosis. Two main types of roentgenographic changes are seen: the nonspecific type, which reveals only increased intracranial pressure, and the specific changes, the most important of which is the presence of calcified cysts. Of the nonspecific, general roentgenographic changes associated with increased intracranial pressure, we frequently observed enlargement of the sella, with erosion and destruction of its floor, dorsum and clinoid processes. The common occurrence of the basilar type seems to be an important factor in the frequent production of changes in the sella. The most specific roentgenographic manifestation of cysticercosis is the presence of multiple, small, diffuse intracranial calcifications, and these we observed in just over one third of our cases. Dixon and Hargreaves observed calcified areas in 11 per cent of their cases.

More rarely, the cysts produce areas of erosion of bone in the cranial vault, which may result in small perforations of the skull, as

seen in case 3. Occasionally one may observe all changes in the same roentgenogram, i.e., enlargement and destruction of the sella, multiple areas of erosion of the skull and small diffuse, multiple intracranial calcifications (case 3).

Encephalographic and ventriculographic studies with air may be of help in the diagnosis. We have usually found dilatation of the lateral ventricles, which may be either symmetric or asymmetric. The third ventricle and the aqueduct may be well filled in some cases, but in others there is no visualization of these structures. Aside from this general picture of hydrocephalus, and contrary to the case with tumors, the air passes through the rest of the subarachnoid space and may fill the cisterna magna and the cisterns at the base of the brain. In many cases pronounced atrophy of the cerebral cortex or cerebellum is shown by a collection of air over the cortex, the cisterna magna and the subtentorial region. In some cases the cortical atrophy is so extreme that in the lateral roentgenograms the lateral ventricles are covered with an air shadow. This association of hydrocephalus and diffuse cerebral atrophy is, in our experience, fairly typical of cysticercosis, and Arana and Asenjo<sup>2</sup> also showed that the characteristic ventriculographic picture of infratentorial cysticercosis consists in hydrocephalus with partial obliteration of the aqueduct and a collection of air in the cisterna magna and around the cerebellum, as a consequence of the cerebellar atrophy.

#### CEREBROSPINAL FLUID IN CASES OF CEREBRAL CYSTICERCOSIS<sup>10</sup>

The cerebrospinal fluid was analyzed in 27 cases; in a great number of these cases the diagnosis of cysticercosis was confirmed by autopsy or operation, while in the others it was based on the clinical picture and the results of analysis of the cerebrospinal fluid.

In the majority of cases of cerebral cysticercosis, nonspecific changes in the cerebrospinal fluid indicated an inflammatory process. There was an increase in the number of cells, which generally varied from 15 to 100 per cubic millimeter. The protein content was also increased but was rarely above 100 mg. per hundred cubic centimeters, and there was also an increase in the globulin. The colloidal gold reaction showed inconsistent modifications, and the Wassermann reaction was always negative. All these nonspecific changes in the cerebrospinal fluid were variable and appeared to depend on the number of cysts and their state of activity in the course of the disease. Other secondary factors, such as possible infection of the cysts, may also influence the cerebrospinal fluid.

10. This section on the cerebrospinal fluid was written by Dr. D. Nieto, who analyzed all his personally collected and studied material.

These nonspecific modifications of the fluid give no definite information as an aid to diagnosis, as they appear with many other inflammatory conditions of the nervous system. Special studies that provide a more specific result are therefore needed. The presence of a significant proportion of eosinophils is important, and other workers, especially Lopez Albo,<sup>4</sup> have stressed this point. The significance of this observation was confirmed in the present series, there being eosinophils in the cerebrospinal fluid in all the 27 cases, the proportion varying from 0.5 to 33 per cent. Although in other parasitic diseases of the nervous system eosinophils may be present in the cerebrospinal fluid, the relative frequency of cysticercosis, especially in Mexico, gave this sign a useful and practical value in the diagnosis of cerebral cysticercosis.

The amount of glucose in the cerebrospinal fluid is generally decreased to below 50 mg. per hundred cubic centimeters. Sometimes the glucose content reaches a very low level. In 1 of my cases the value was only 5 mg., and in a case reported by Lopez Albo<sup>4</sup> there was no sign of the sugar in the cerebrospinal fluid. The low glucose content, although frequent, is not a constant sign, and in some of the present cases values were normal. Thus, this change, when it is present, has great importance, especially since cerebral cysticercosis is the only chronic disease of the nervous system in which low values can be found for glucose in the cerebrospinal fluid.

The more important characteristic of the fluid, however, is the specific reaction to the complement fixation test. This test was originally used, with inconstant results (Weinberg); but more recently, in Brazil, it has been used by Lange with good results. My colleagues and I have been using this test since 1942, and in our experience a positive reaction has proved to be the most important and specific observation in the diagnosis of cerebral cysticercosis. We use a total alcoholic extract of pig cysticerci as an antigen, the preparation and proper titration of which I shall describe in another publication. The technic of the test is the same as that of the Wassermann test of the cerebrospinal fluid, constant doses of antigen and variable amounts of fluid being used. In our material of 27 cases, the reaction was positive with 1 cc. in 2 cases, with 0.5 cc. in 10 cases and with 0.2 cc. in 15 cases.

In some cases we made a comparative study of the lumbar and ventricular fluids. The alterations were always less pronounced in the ventricular fluid, as is seen with other neurologic diseases. The proportion of eosinophils, however, was about the same in the lumbar and in the ventricular cerebrospinal fluid. The complement reaction of the ventricular fluid was always weaker than that of the lumbar

fluid; for example, in 1 case the reaction was positive with 0.2 cc. of the lumbar fluid and with 1 cc. of the ventricular fluid.

A careful study of the cerebrospinal fluid is the best, and in many cases the only, method for the diagnosis of cerebral cysticercosis. In addition to some general inflammatory and nonspecific signs, there are certain specific findings, such as the reaction to the complement fixation test with specific antigen. The presence of eosinophils is a useful and important sign and may lead one to suspect cysticercosis. A low sugar content, although not constant, is significant when it is present. We consider the analysis of the cerebrospinal fluid the most important investigative method in the diagnosis of cysticercosis, especially in view of the difficulties of the diagnosis on clinical grounds alone. This view is opposed to that expressed by Dixon and Hargreaves,<sup>5</sup> who, in agreement with MacArthur,<sup>6</sup> stated that any deviation from the normal in the cerebrospinal fluid is of no positive diagnostic significance and that the fluid usually remains unaffected. The difference of material may be responsible for such a difference of opinion, as the present cases were selected for study because of their obvious neurologic symptoms.

Dr. M. Fuentes provided the records and information on some of his cases and on several cases which we studied together.

## MODIFICATION BY CURARE OF CIRCULATORY CHANGES DURING ELECTRICALLY INDUCED CONVULSIONS IN MAN

A Note on D-Tubocurarine

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THE EFFECTS of convulsions induced by electroshock on the circulation have been studied by several authors. The changes consist in elevation of venous pressure,<sup>1</sup> acceleration of circulation time,<sup>2</sup> a rise, followed by a fall, in arterial pressure<sup>3</sup> and changes in cardiac rhythm indicative of vagal hyperactivity.<sup>4</sup> Since curare is widely used to decrease the severity of the seizures induced in the treatment of mental disease, it was considered important to ascertain the manner in which premedication with that drug influences the circulatory changes which are the consequence of convulsant therapy. Work on arterial pressure already reported by Cleckley and associates<sup>3b</sup> has shown that rises in blood pressure during induced convulsions are diminished when patients are curarized; accordingly, the present study has been confined to observations on the venous pressure and the electrocardiogram.

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From the Clinical Services of the McLean Hospital, Waverley; the Medical Research Laboratories of the Beth Israel Hospital, Boston, and the Departments of Psychiatry and Medicine of the Harvard Medical School.

1. (a) Silfverskiöld, B. P., and Aemark, C.: Disturbance of Circulation in Convulsions of the Epileptic Type: II. Arterial and Venous Pressure During Electroshock, *Acta med. Scandinav.* **113**:191, 1943. (b) Altschule, M. D.; Sulzbach, W. M., and Tillotson, K. J.: Effect of Electrically Induced Convulsions on Peripheral Venous Pressure in Man, *Arch. Neurol. & Psychiat.* **58**:193 (Aug.) 1947.

2. Altschule, M. D.; Sulzbach, W. M., and Tillotson, K. J.: Significance of Changes in the Electrocardiogram After Electrically Induced Convulsions in Man, *Arch. Neurol. & Psychiat.*, to be published.

3. Silfverskiöld and Aemark.<sup>1a</sup> Cleckley, H., Hamilton, W. P.; Woodbury, R. A. and Volpitta, P. D.: Blood Pressure Studies in Patients Undergoing Convulsive Therapy, *South. M. J.* **35**:375, 1942.

4. Altschule and others.<sup>2</sup> Bellet, S.; Kershbaum, A., and Furst, W.: The Electrocardiogram During Electric Shock Treatment of Mental Disorders. *Am. J. M. Sc.* **201**:167, 1941.

## MATERIAL AND METHODS

Ten patients with depressions, 8 of them women, were studied. The ages ranged from 39 to 79, but only 1 was less than 57 years old; the average age was 65. Observations were made during 88 electroshock treatments.

After the patients were brought to the treatment room and placed on the table for treatment in the routine manner, electrodes were placed for standard three-lead electrocardiograms; a 19 gage needle was then inserted in an antecubital vein for measurement of the venous pressure, as previously described.<sup>1b</sup> Electrocardiograms were made before and after the injection of curare and again at the end of the seizure; the venous pressure was observed continuously for a period beginning several minutes before the injection of curare and ending forty-five to sixty seconds after cessation of the convulsion.

The curare was injected intravenously in doses of 0.4 to 0.55 unit per pound of body weight, the period of injection being sixty to seventy seconds; seizures were induced not less than one or more than three minutes after the end of injection. Two preparations of curare were used: "intocostrin" and a solution of *d*-tubocurarine; the former was used in 27 treatments, with 4 patients, and the latter in 61 treatments, with 7 patients. One patient received each of the two preparations on several occasions.

## OBSERVATIONS

*Venous Pressure.*—The initial venous pressure levels were normal in 78 experiments, i.e., they ranged from 4 to 10 cm. of water. In 5 patients, however, initial readings of from 11 to 20 cm. were found in 10 of the total of 44 studies performed on these patients. After

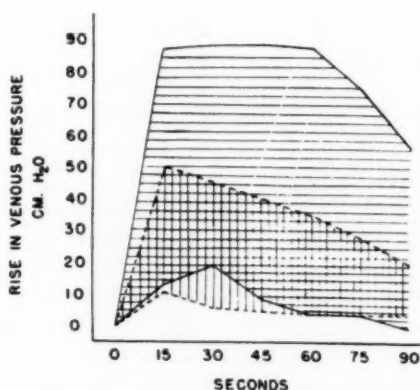


FIG. 1.—Range of increase in venous pressure during seizures in curarized (crosshatched area) and uncurarized (area of lines) patients.

the injection of curare in these instances the venous pressure fell to normal limits. In 33 other instances, in which the initial readings were in the normal range, decreases of 1 to 5 cm. also occurred. The average of all the decreases in venous pressure was 2.5 cm. of water. Whatever diminution in venous pressure occurred after curare was

associated with visible relaxation from a state of abnormal muscular tension.

When the convulsion began, after the induction of electric shock, the venous pressure rose. The initial rise was between 11 and 50 cm. and averaged 23 cm. In 42 experiments the rise continued as the seizure persisted, whereas in 46 experiments the immediate rise was followed by a decline. The degree of increase in venous pressure was visibly related to the violence of the seizure; the degree of rise was usually half as great as in uncurarized patients, but a good deal of overlapping of values was found (figs. 1 and 2). The convulsions were on the average approximately twelve seconds longer than seizures

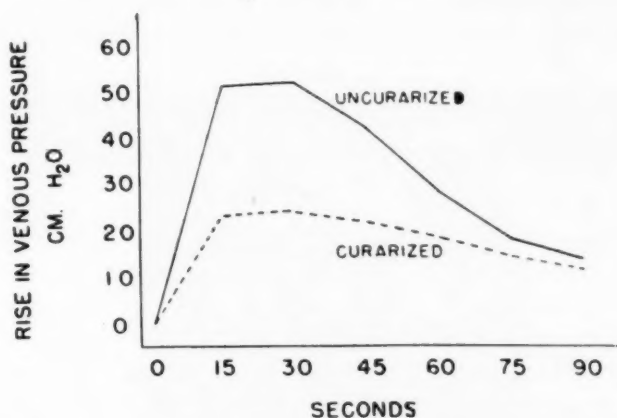


FIG. 2.—Average increase in venous pressure during seizures in curarized and uncurarized patients.

induced without curarization; at the end of the seizure the venous pressure was still somewhat above the control level (fig. 1).

*Electrocardiograms.*—Before treatment the electrocardiograms of all but 1 patient showed abnormalities (table); ventricular premature beats were found in 4 patients. After the injection of curare no

*Pretreatment (Control) Electrocardiographic Patterns*

Case	ELECTROCARDIOGRAPHIC FEATURES
1	Left axis deviation; low T wave in lead III; ventricular premature beats
2	Inverted T wave in lead I
3	Left axis deviation; low T waves in leads I and II
4	Left axis deviation; flat T wave in lead III; depressed S-T interval in leads II and III; ventricular premature beats
5	Normal
6	Flat T wave in lead III
7	Low T wave in lead I; ventricular premature beats
8	Left axis deviation; matched QRS; low T waves in all leads; depressed S-T interval in leads I and II; sinus bradycardia.
9	Depressed S-T interval in leads II and III; prominent Q waves in lead III; ventricular premature beats
10	Low T wave in lead I; prominent S waves in all leads

changes in rhythm or in electrocardiographic pattern were observed; inconstant and variable changes in cardiac rate occurred. After the

cessation of the induced convulsion arrhythmias were noted in all patients: In 1 patient they were present during only 4 of 7 seizures and in another during 6 of 14 seizures; in all the remaining patients they occurred after every seizure. Sinus arrhythmia was found to occur in every patient after from 22 to 100 per cent of the convulsions. Sinus bradycardia occurred in 2 patients, once in 1 patient and after half the seizures in the other. Auricular premature beats were noted in 6 patients, once in each of 2 patients, during 2 to 4 seizures in 3 patients, and during 8 seizures (in a total of 10) in the sixth patient. In the last patient these premature beats were of interest in that usually each was followed by a somewhat aberrant ventricular complex suggestive of right bundle branch block (fig. 3*A*). Nodal beats occurred in 6 patients after 9 to 50 per cent of the seizures; 4 of the 6

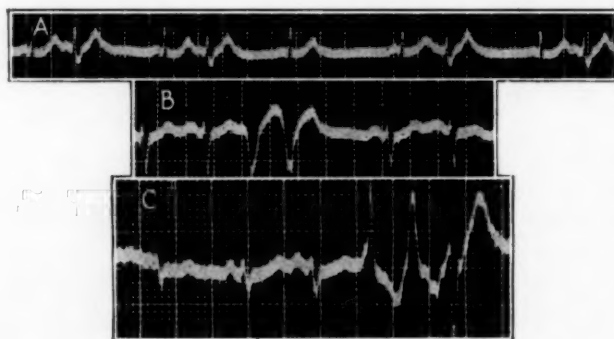


Fig. 3.—*A*, Auricular premature beats followed by aberrant QRS complexes; *B*, ventricular premature beats; *C*, ventricular premature beats arising from different foci, with variation in size of the QRS complexes associated with respirations.

patients with nodal premature beats also had auricular premature beats. Ventricular premature beats occurred in 7 patients, once each in 5 patients and after 75 and 100 per cent of the seizures, respectively, in the other 2 patients (fig. 3*B* and *C*). In 1 of the last patients the ventricular extrasystoles arose from different foci and often occurred in groups, with a rate of approximately 300 (fig. 3*C*). The 2 patients who showed many ventricular extrasystoles after seizures had them occasionally in the control tracings.

A rhythmic variation in the size of the QRS complexes, greatest in leads I and III, occurred in all instances; this was correlated with hyperpneic respiration. Minimal depression of the S-T interval occurred in one or more leads after most seizures; this never exceeded 2 mm.

#### COMMENT

Curare as used clinically does not abolish the convulsion in electroshock therapy. The seizure, though weaker, is still present and is

actually prolonged in most instances. In accord with the lessened violence of muscular contractions observed in seizures induced electrically after injection of curare, rises in venous pressure were relatively small (figs. 1 and 2). However, some rise occurred during every experiment. It was pointed out previously that increases in venous pressure raise filtering pressures in the small vessels and give rise to hemoconcentration.<sup>5</sup> It is to be expected that hemoconcentration would be lessened when convulsions are made less violent by means of curare; a few experiments<sup>5</sup> support this concept. In earlier work<sup>1b</sup> the hazards of excessive increases in venous pressure in elderly patients and in patients with cardiac disease were pointed out; curare appears to be a means of diminishing these untoward reactions to electroshock therapy.

In agreement with the observations of Ruskin and associates,<sup>6</sup> curare itself in the doses used caused no change in the electrocardiogram. The electrocardiographic changes which were found after convulsions in the present study were in general similar to those previously described in uncurarized patients; i.e., minor degrees of depression of the S-T interval, increase in size of the P waves, a rhythmic variation in size of the QRS complexes and a variety of vagal arrhythmias were noted. However, the last change, though found after as many convulsions in curarized as in uncurarized patients, was usually not so pronounced in the curarized patients. The presence of a lessened degree of arrhythmia induced by vagal influences in association with a lessened rise in venous pressure in seizures induced after the administration of curare suggests that these arrhythmias are at least partly reflex in origin. The return to normal of the increased intrapleural pressure associated with the convulsion causes the blood impounded in the extremities during the seizure to flow rapidly into the great thoracic veins and right auricle and thereby to stimulate the vagus nerve. As the violence of the convulsion is diminished, the intrapleural pressure rises less, and so less blood is impounded in the peripheral veins; relaxation is followed by a return of this lesser amount of blood to the heart, and a lesser degree of vagal stimulation results.

In a previous work<sup>7</sup> it was pointed out that some of the untoward

5. Altschule, M. D.; Cram, J. E., and Tillotson, K. J.: Hemoconcentration After Electrically Induced Convulsions in Man, *Arch. Neurol. & Psychiat.* **59**:29 (Jan) 1948.

6. Ruskin, A.; Ewalt, J., and Decherd, G.: The Electrocardiogram of Curarized Human Subjects, *Dis. Nerv. System* **4**:335, 1943.

7. Altschule, M. D., and Tillotson, K. J.: Untoward Reactions to Curare Consequent to Vagal Hyperactivity Occurring After Electrically Induced Convulsions in Man, *Arch. Neurol. & Psychiat.* to be published.

reactions to "intocostrin" are apparently consequent to excessive activity of the vagus nerve, while the present study indicates a lessened degree of vagal hyperactivity after seizures in curarized patients. These two observations are not incompatible with each other, for it was concluded<sup>7</sup> that when the severe vagal type of reaction to "intocostrin" occurred it was apparently consequent to impurities present in some of the lots of the drug and was not caused by the active alkaloid, *d*-tubocurarine, itself.

The occurrence of ventricular premature beats was commoner in curarized than in uncurarized patients after convulsions; indeed, in 1 patient of the former group the premature beats arose from different foci and presented the electrocardiographic features of brief periods of ventricular tachycardia, a potentially dangerous arrhythmia. The significance of this phenomenon is not clear, for the average age of the patients in this series was 65, as compared with 39.6 for the uncurarized patients previously reported.<sup>1b</sup> Moreover, the 2 patients of the present study who showed ventricular premature beats in large numbers after almost every seizure also had occasional ventricular extrasystoles in tracings made before induction of the convulsions. A tentative suggestion might be that elderly patients who exhibit electrocardiographic evidence of frequent ventricular extrasystoles after seizures should be given 0.2 to 0.3 Gm. of quinidine sulfate U.S.P. one hour before each treatment.

The effectiveness of a given dose of *d*-tubocurarine was indistinguishable from that of the same dose of "intocostrin." In 1 patient, however, a striking difference between the two was apparent in that "intocostrin" on each of 4 occasions caused an alarming degree of respiratory difficulty with wheezing and cyanosis, whereas *d*-tubocurarine in the same dose caused no such reaction except for a slight wheeze on 1 of the 6 occasions on which it was used in this case. During none of the other 60 treatments of 6 patients did *d*-tubocurarine cause any untoward reaction. In another patient, not included in this series, a seizure was induced on 1 occasion after the intravenous injection of *d*-tubocurarine in the usual dose; the convulsion was followed by the development of delayed apnea, requiring the intratracheal administration of oxygen and 5 per cent carbon dioxide for thirty minutes. Recovery thereafter was immediate and complete. Other complications were observed in 2 patients of the present study; an abscess of the lung developed in 1 patient and a small fracture of a thoracic vertebra occurred in another.

#### SUMMARY AND CONCLUSIONS

The administration of curare before induction of convulsive seizures reduces the degree of rise in venous pressure caused by convul-

sions; changes in the electrocardiograms of curarized patients given electroshock therapy are similar to, but generally less prominent, than those of uncurarized patients. An apparent exception is the frequent occurrence of ventricular premature beats after seizures in curaried patients; this finding is difficult to evaluate, since the patients of the present study were for the most part well advanced in years. It is concluded also that *d*-tubocurarine has all the effectiveness of "intocostin" and lacks some of its drawbacks.

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## FALL IN PLASMA PROTEIN LEVEL ASSOCIATED WITH RAPID GAIN IN WEIGHT DURING COURSE OF ELECTROSHOCK THERAPY

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**R**EMISSIONS induced by electroshock therapy in patients with depressions are usually ushered in by a gain in body weight. The mechanism of this gain in weight is obscure; the present study has been designed to throw light on this problem.

### MATERIAL AND METHODS

Nine patients, 5 of them men, were studied. The ages ranged from 21 to 57 years. Hematocrit readings and determinations of plasma protein levels were made three times a week, the latter by the copper proteinate method,<sup>1</sup> using blood drawn without stasis when the patient was in the postabsorptive state. The patients were also weighed to the nearest pound on the days of these determinations.

The diagnoses are tabulated as follows:

Case	
G	Involitional depression
Ba	Paranoid state; reactive depression
Be	Manic-depressive psychosis, depressed
T	Compulsive-obsessive neurosis; reactive depression
D	Anxiety neurosis; reactive depression
N	Compulsive-obsessive neurosis
Ma	Manic-depressive psychosis, depressed
Mc	Manic-depressive psychosis, depressed
W	Psychoneurosis; reactive depression

### OBSERVATIONS

*Patients Who Gained Weight.*—Five patients, all of whom showed good clinical improvement during the course of electroshocks, gained 3 to 7 pounds (1.3 to 3.2 Kg.) during the period of treatment (fig. 1; table). For all of them the plasma protein level, initially within the normal range, decreased during the period of most rapid gain in weight (fig. 1; table). The maximal decreases in plasma protein level during the period of rapid gain in weight ranged from 0.43 to 1.30 Gm. per hundred cubic centimeters for each patient, with an average

From the Clinical Services of the McLean Hospital, Waverley; the Medical Research Laboratories of the Beth Israel Hospital, Boston, and the Departments of Psychiatry and Medicine of the Harvard Medical School.

1. Phillips, R. A.; Van Slyke, D. D.; Doyle, V. P.; Emerson, K., Jr.; Hamilton, P. B., and Archibald, R. M.: Copper Sulphate Method for Measuring Specific Gravities of Whole Blood and Plasma, Bull. U. S. Army M. Dept., 1943, no. 71, p. 66.

*Observations on Nine Patients with Remissions Induced by Electroshock Therapy*

Case	Day of Study	Weight, Lb.	Plasma Protein Gm. 100 Cc.	Hematocrit, % Cells	Treatment No. on Day of Study
G	1	83	6.65	48	1
	3	84	5.81	44	2
	6	85	5.64	41	3
	8	88	5.47		4
	10	89	5.37		
Ba	1	157	6.49	48	1
	4	160	6.30	47	2
	6	160	5.81	44	3
	8	160	6.38	45	4
	11	160	6.08	45	5
	13	160	5.50	45	
Be	1	155	6.51		1
	3	155	6.51	48	2
	6	156	6.25	49	3
	8	158	6.08	46	4
	10	158	6.51		5
	13	159	6.35	49	6
	15	159	6.27	48	
T	1	182	7.18		1
	3	184	6.83		2
	6	186	6.51	49	3
	20	181	7.16	50	
				52	
D	1	122	7.33	45	1
	3	123	7.18	44	2
	6	123	7.40	46	3
	8	127	6.88	43	4
	10	127	7.06	44	5
	13	126	7.62	46	6
	15	128	6.65	42	7
	17	129	7.05	44	
N	1	97	6.17	48	1
	4	95	6.49	48	2
	6	97	6.17	46	3
	8	97	6.00	48	4
	11	96	6.35	50	5
	13	96	6.19	48	6
	15	96	6.77	50	7
	18	96	6.28	48	8
	20	96	6.28	48	9
	22	96	6.49	50	
Ma	1	132	6.12	45	1
	3	132	6.27	46	2
	5	129	6.35	46	3
	8	129	6.41	46	4
	10	130	6.49	42	
Mc	1	157	6.65	42	1
	3	157	6.77	44	2
	6	157	6.92	44	3
	8	157	6.71	42	4
	10	156	6.69	40	
W	1	160	6.65	46	1
	3	158	6.74	43	2
	5	157	6.74	44	3
	8	156	7.16	48	4
	10	156	6.71	46	

of 0.71 Gm. per hundred cubic centimeters (fig. 1; table). One patient (table, case F) maintained neither the clinical improvement nor the gain in weight (fig. 1), and the plasma protein level, after a fall, rose to its initial level. Three others (fig. 1; table, cases Ba, Be and D) showed a rise in the plasma protein level after its initial de-

crease in spite of the fact that the gain in weight was maintained. For the remaining patient (table, case G), showing persistent gain in

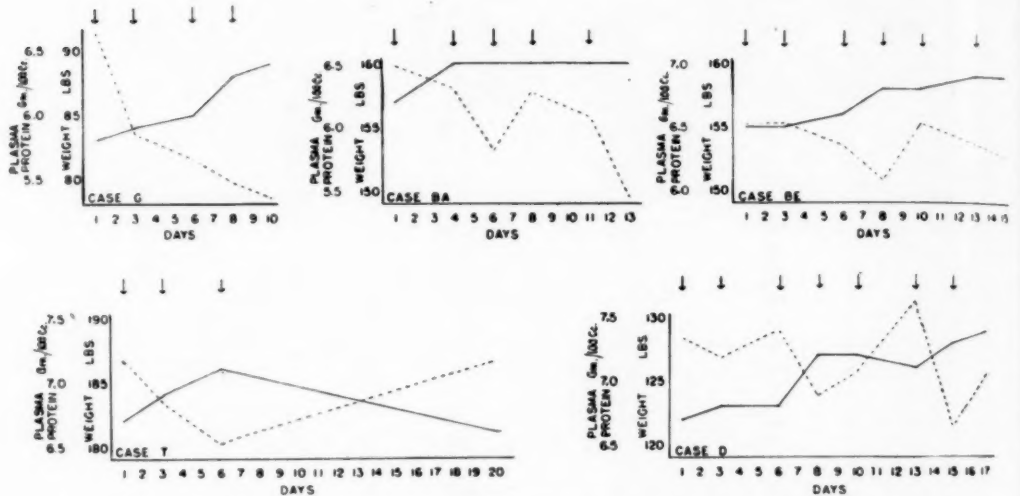


Fig. 2.—Changes in plasma protein level in patients who failed to gain weight. In this figure, and in figure 2, the plasma protein levels, expressed in grams per hundred cubic centimeters, are represented by the dotted lines; the weights, in pounds, by the solid lines. The arrows indicate shock treatments.

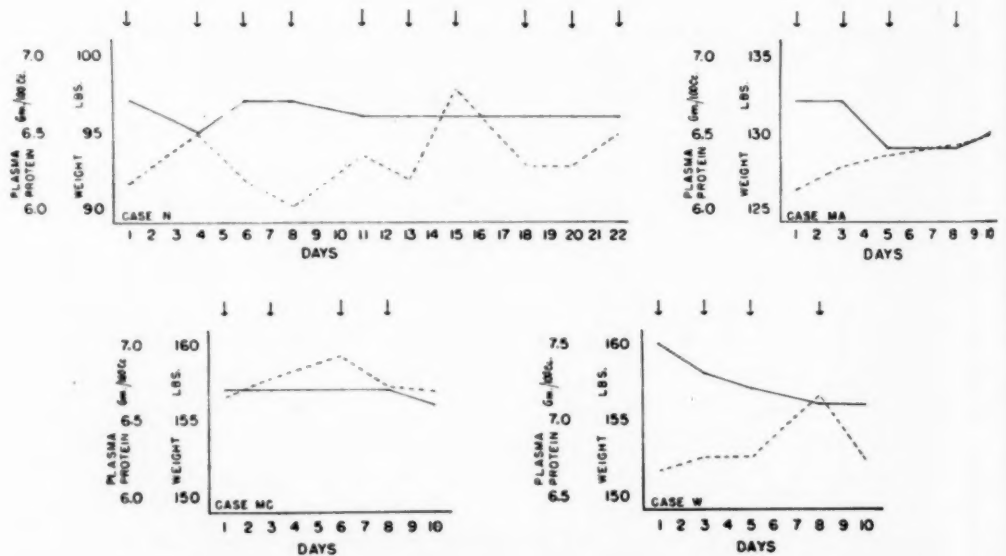


Fig. 2.—Changes in plasma protein level in patients who failed to gain weight.

weight and clinical improvement (fig. 1), the period of study was too short to permit the detection of a secondary rise in plasma protein levels.

Except in case G, in which a decrease in the hematocrit reading of 15 per cent was associated with the gain in weight, no significant changes were found in this measurement (table).

*Patients Who Failed to Gain Weight.*—Four patients (table; cases N, Ma, Mc and W), none of whom showed striking clinical improvement during the period of study, gained no weight, or actually lost, during the period of treatment. Their plasma protein levels fluctuated, with no trend toward a decrease (fig. 2); if anything, an increase occurred in several cases. The hematocrit reading showed no significant changes for any of these patients (table). Two of them (cases Ma and Mc) showed improvement at a later date, when additional electroshock treatments were given after the termination of this study.

#### COMMENT

The lowering of the plasma protein level which may occur in patients receiving electroshock therapy suggests the possibility of hemodilution. The question whether this phenomenon might be related to antecedent dehydration consequent to the dementia must be considered. In the group of patients here discussed, as well as many others seen in clinical practice, the occurrence of such dehydration, though common, is far from uniform. Thus, of the patients in the present study, dehydration was considered to be present on the basis of the history and physical findings in only 1 (case G), the patient who exhibited the largest gain in weight and the greatest degree of hemodilution. This patient was the only one to show a significant fall in the hematocrit reading with the gain in weight. The correction of antecedent dehydration is one of the consequences of remission due to electroshock therapy but accounts only in part for the fall in plasma protein level. Another explanation of the observed changes in plasma protein occurring in association with gain in weight might be retention of water beyond that necessary to correct dehydration. Since such retention of water in the form of an increase in the volume of extracellular fluid does occur during the course of electroshock therapy,<sup>2</sup> it is possible that the decreases in plasma protein level here described may be consequent to hemodilution. However, the absence of consistent significant changes in hematocrit values is against this concept.

On the other hand, another mechanism for the decrease in plasma protein concentration might be a loss of protein from the blood into the tissues. An increase in the volume of extracellular fluid occurs during the course of electroshock therapy,<sup>2</sup> and this fluid must contain some protein; the source of this protein might well be the blood in

2. Altschule, M. D.; Ascoli, I., and Tillotson, K. J.: Changes in Extracellular Fluid and Plasma Volumes During the Course of Electroshock Therapy, to be published.

poorly nourished patients with inadequate stores of tissue protein. In a previous study,<sup>3</sup> it was pointed out that the high intravascular pressures which develop during each electrically induced convulsion may cause the loss of protein together with the fluid which leaves the plasma. This loss, however, was rapidly corrected after each treatment, and, moreover, occurred during each convulsion, so that the pattern of change in plasma protein level consequent to the high filtering pressures occurring during each seizure was quite different from that observed in the present study.

Of great interest is the fact that the pattern of variation in plasma protein, i.e., a transitory fall in plasma protein level, found here is identical with that reported by Abels, Young and Taylor<sup>4</sup> in previously depleted patients who gained weight and stored protein during the course of a series of injections of androgens.<sup>3</sup> It appears, therefore, that the variations in plasma protein found in the present study during the course of electroshock therapy probably indicate the onset of a period of storage of tissue protein. The occurrence together of gain in weight, water retention<sup>2</sup> and the variations in plasma protein level here described during the course of electroshock therapy is strongly suggestive of the effects of a change in steroid metabolism. That such a change does occur in patients receiving electroshock has been reported by other authors.<sup>5</sup> Gain in weight ushers in clinical recovery in a large majority of cases. However, neither the present work nor any investigation previously recorded in the literature establishes the mechanism of remission of mental illness following convulsant therapy. For the present, it can be stated only that clinical recovery and physiologic changes suggestive of the action of metabolic influences occur at the same time.

#### SUMMARY AND CONCLUSIONS

A transitory decrease in plasma protein level accompanies the gain in weight which ushers in clinical improvement in patients receiving electroshock therapy. The correction of dehydration accounts only in part for this change. The studies suggest the occurrence of a transitory loss of protein from the circulation, and the pattern of change is that which occurs in patients who, after a period of depletion, begin to store tissue protein.

McLean Hospital.

3. Altschule, M. D.; Cram, J. E., and Tillotson, K. J.: Hemoconcentration After Electrically Induced Convulsions in Man, *Arch. Neurol. & Psychiat.*, **59**:29 (Jan.) 1948.

4. Abels, J. C.; Young, N. F., and Taylor, H. C.: Effects of Testosterone and of Testosterone Propionate on Protein Formation in Man, *J. Clin. Endocrinol.* **4**:198, 1944.

5. Hoagland, H.; Malamud, W.; Kaufman, I. C., and Pincus, G.: Changes in the Electroencephalogram and in the Excretion of 17- Ketosteroids Accompanying Electro-Shock Therapy of Agitated Depression, *Psychosom. Med.* **8**:246, 1946.

## REFLEX STUDIES IN ELECTROSHOCK TREATMENTS

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**D**URING administration of extramural electroshock therapy, special attention was paid to the problem of reflex changes following treatments. Various investigators have repeatedly pointed out the frequent presence of tendon hyperreflexia, ankle clonus and a Babinski sign following electroshock convulsions. Kino<sup>1</sup> alone noted frequent plantar areflexia for a short period before the appearance of the Babinski sign. We observed an unusually high incidence of plantar areflexia without a Babinski sign after such treatments. This finding is of considerable theoretic importance because it brings up the significant question whether the electroshock convulsion is physiologically identical with the epileptic seizure, since the latter is almost always followed by a Babinski sign.

Five hundred treatments were administered to 79 patients between the ages of 25 and 58 years. The patients were examined before treatment, immediately after the induced convulsions and at short intervals thereafter. There were 59 patients with manic-depressive psychosis, 12 with schizophrenia, 4 with involutional melancholia and 1 with a reactive depression associated with psychoneurosis. Before treatment, normal plantar responses were encountered in 418 tests, poor plantar responses in 58 tests and a Babinski sign in 21 tests; in 3 instances the same patient showed a unilateral Rossolimo sign.

Each patient showed transitory hyperreflexia in the lower limbs for one to two minutes immediately after treatment. In 90 per cent of the patients ankle clonus was present. A Rossolimo sign was never seen after a convulsion. The reflex changes were not always the same after each treatment. Kino stated that the same reflex changes recurred after each treatment, but some of our patients showed a Babinski sign after some treatments and plantar areflexia after others.

F. S. had five treatments. After the second she showed a Babinski sign on the right side, whereas after the other four treatments plantar areflexia was present for eight to ten minutes.

1. Kino, F. F.: Reflex Studies on Electric Shock Procedure, *Brain* **66**:152, 1943.

L. B. showed plantar areflexia after the first treatment and a bilateral Babinski sign for twelve and ten minutes, respectively, after the second and third treatments.

G. G. showed a bilateral Babinski sign following plantar areflexia after eight treatments and only plantar areflexia after two treatments.

I. M. showed postconvulsive plantar areflexia after three treatments and a bilateral Babinski sign after five other treatments.

The Rossolimo reflex noted prior to treatment in 1 case disappeared each time after the convulsion, with appearance of plantar areflexia for two minutes, followed by a bilateral Babinski sign for the same period.

In 18 instances normal plantar flexion was elicited after electrically induced petit mal attacks. This finding indicates that the abnormal reflexes following the treatments are probably sequelae of the convulsions, rather than of the passage of the current through the brain.

Plantar areflexia immediately following the convulsion was noted in 469 treatments (93.8 per cent). After 341 treatments plantar areflexia alone was observed; after 128 treatments the plantar areflexia was followed by a bilateral Babinski sign; after 7 treatments a Babinski sign was seen without preceding plantar areflexia; after 5 treatments (1 per cent) the reflexes could not be tested for, owing to lack of cooperation on the part of the patient. We did not find any difference in response during the period of plantar areflexia to stimulation of the inner and outer aspects of the sole.

The postconvulsive plantar areflexia lasted two to eighteen minutes. In all 12 instances in which a bilateral Babinski sign was present before treatment, plantar areflexia, lasting two to five minutes, followed the seizure. The Babinski sign reappeared each time. One patient with a petit mal reaction showed poor plantar response on the left and a Babinski sign on the right before and after the treatment.

Kino,<sup>1</sup> Fleischhacker,<sup>2</sup> Ramirez Moreno<sup>3</sup> and Impastato and Almansi<sup>4</sup> noted the frequency of hyperreflexia, clonus and the Babinski sign following electric shock treatments. Kalinowsky and Kennedy<sup>5</sup> noted a Babinski sign in less than one third of all cases but did not describe the plantar response in the other two thirds. Kino<sup>1</sup> found plantar areflexia for a few minutes after the treatment, but it was always followed by a

2. Fleischhacker, H. H.: Some Neurological and Neurovegetative Phenomena Occurring During and After Electro-Shock, *J. Nerv. & Ment. Dis.* **102**:185 (Aug.) 1945.

3. Ramirez Moreno, S.: Tratamiento por electrochoques, *Rev. mex. psiquiat, neurol. y med. leg.* **10**:3 (Jan.) 1944.

4. Impastato, D. J., and Almansi, R.: Electrically Induced Convulsions in the Treatment of Functional Mental Disease, *M. Ann. District of Columbia* **10**:163 (May) 1941.

5. Kalinowsky, L. B., and Kennedy, F.: Observations in Electric Shock Applied to Problems of Epilepsy, *J. Nerv. & Ment. Dis.* **98**:56, 1943.

Babinski sign. No investigator noted, as we did, a prolonged plantar areflexia which was not followed by a Babinski sign or any of its confirmatory reflexes. We cannot confirm the observation of Kino<sup>1</sup> that patients with brisk plantar flexion before treatment show a strong Babinski reflex afterward.

There is no unanimity of opinion on the clinical significance of plantar areflexia. Goldflam,<sup>6</sup> who was apparently the first to discuss the clinical value of this sign, expressed the belief that it was due to a central lesion, that it had about the same significance as the abdominal and cremasteric reflexes and that it appeared before the Babinski sign with lesions of the corticospinal tracts. Lewandowsky<sup>7</sup> and Oppenheim<sup>8</sup> stated that it had no clinical significance. Walton and Paul<sup>9</sup> recorded that the plantar response is absent on one side in 10 per cent of normal people—a fact that was not confirmed by Kino.<sup>1</sup> The latter reported that the plantar response is absent bilaterally in 10 per cent of normal people. He also stated that plantar areflexia is the earliest sign of involvement of the pyramidal tract. Minkowski,<sup>10</sup> on the basis of clinical experience and studies of the dying fetus, stated the belief that plantar areflexia is evidence of severe injury to the cord. Dejerine,<sup>11</sup> Babinski and Froment<sup>12</sup> and others noted the absence of plantar response in cases of hysteria. We have observed absence of the plantar reflex on the side of a functional hemisensory syndrome in many cases.

The recent work of Gley and his associates<sup>13</sup> suggests that electroshock convulsions are physiologically different from convulsions induced by electrical stimulation of the cortex. The high incidence of plantar areflexia in the present study also suggests that during electroshock changes

6. Goldflam, S.: Ueber Abschwachung bzw. Aufhebung des Sehen-und Verkürzungsreflexes, *Neurol. Centralbl.* **27**:946, 1908.

7. Lewandowsky, M.: *Die Kriegschaden des Nervensystems und ihre Folgeerscheinungen*, Berlin, Julius Springer, 1919, p. 5.

8. Oppenheim, H.: *Lehrbuch der Nervenkrankheiten*, ed. 7, Berlin, S. Karger, 1923.

9. Walton, G. L., and Paul, W. E.: Contribution to the Study of the Plantar Reflex Based upon Seven Hundred Examinations Made with Special Reference to the Babinski Phenomenon, *J. Nerv. & Ment. Dis.* **27**:305, 1900.

10. Minkowski, M.: *L'état actuel de l'étude des reflexes*, Paris, Masson & Cie, 1927.

11. Dejerine, J.: Sur l'abolition du réflexe cutané plantaire dans certains cas de paralysies fonctionnelles accompagnées d'anesthésie: Hystéro-traumatisme, *Rev. Neurol.* **22**:521, 1914-1915.

12. Babinski, J., and Froment, J.: Abolition du réflexe cutané plantaire, anesthésie associées à des troubles vaso-moteurs et à de l'hypothermie d'ordre réflexe, *Rev. neurol.* **23**:918, 1916.

13. Gley, P.; Lapipe, M.; Rondepierre, J.; Horande, M., and Touchard, T.: Etude expérimentale et comparative de l'électrochoc et de l'épilepsie corticale, *Rev. neurol.* **77**:57 (March-April) 1945.

take place in the brain which differ from those encountered in idiopathic or cortical epilepsy. The longer duration of the seizures in idiopathic and symptomatic epilepsy may be important in accounting for the differences in these reflex changes.

#### CONCLUSION

1. Plantar areflexia followed electroshock convulsions in 93.8 per cent of 500 treatments.
2. In 25.6 per cent of the 500 treatments a Babinski sign was noted after short, variable intervals of plantar areflexia.
3. Petit mal seizures were not followed by any change in the plantar responses.

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## MODIFICATION OF MENINGEAL SIGNS BY CONCOMITANT HEMIPARESIS

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### SIGNS OF MENINGEAL IRRITATION

SINCE Kernig's description<sup>1</sup> in 1907 of a localized sign pointing to meningeal disease, there has been a constantly increasing body of knowledge concerning such phenomena. It was evidently Kernig's early belief that the "leg sign" which he first described was a specific finding for epidemic cerebrospinal meningitis. This early belief was, of course, unfounded, and Kernig later corrected his statement, since the reaction is present in many other varieties of meningeal irritation. Many different, but related, signs of meningeal irritation have since been described, although none is of greater clinical importance than the Kernig leg sign. The purpose of this presentation is to point out the modification of the meningeal sign which frequently occurs when hemiparesis and meningeal irritation are present concomitantly. The recognition of this modification is of clinical importance, as will be shown. In addition, a study of the modification sheds further light on the poorly understood neurophysiologic mechanisms on which the occurrence of the meningeal signs depends.

The Kernig leg sign was often described for a patient in the sitting position with his legs dangling over the side of the bed. If one leg is then passively extended on the thigh, a certain amount of reflex contraction of the hamstring muscles will prevent full extension in the patient with meningeal irritation. Since many patients with meningeal irritation are too ill to sit comfortably on the side of the bed, a modified version of the test is more commonly used to elicit the sign. The patient lies supine in bed while one leg is lifted passively so that the thigh is at right angles to the trunk and the leg is at right angles to the thigh. With the thigh in this position, passive extension of the leg on the thigh is attempted. In the patient with meningeal irritation the extension will be halted by contraction of the hamstring muscles. In addition to the limitation of passive extension of the leg, other phenomena occur with regularity.

1. Kernig, W.: Ueber die f. Beugekontraktur im Kniegelenk bei Meningitis, *Ztschr. f. klin. Med.* **64**:19, 1907. This paper describes the modification of the Kernig sign associated with hemiparesis, and priority for its discovery belongs to its author.

They are flexion at the contralateral hip and knee joint and pain in the back and down the passively raised leg. Brudzinski's leg sign<sup>2</sup> consists of passive flexion of the straight leg until it is halted by reflex contraction of the hamstring muscles. Here, too, in the presence of meningeal irritation there are flexion at the contralateral hip and knee joints and pain.

Similar, although less dependable, signs of meningeal irritation have been described in the upper extremities by Bikeles<sup>3</sup> and others. With the patient sitting, the elbow is passively flexed. The arm is then passively pulled up and back at the shoulder joint to the extreme position. In some cases of meningeal irritation an attempt to extend the elbow joint passively at this point will result in a contraction of the biceps brachii, which will limit this movement of extension. The sign is clinically of little diagnostic significance.

Brudzinski,<sup>2</sup> among others, also described a "neck sign" in meningeal irritation. With the patient lying supine, the head is passively flexed toward the chest. Both thighs and knees may be observed to flex as a result of this maneuver. Many other signs, such as rigidity or retraction of the neck (dorsiextension), tonic neck reflexes, retraction of the abdomen and opisthotonos, have been described as being more or less pathognomonic of meningeal irritation, but these are not germane to the purposes of this paper.

#### CAUSES OF MENINGEAL IRRITATION

Meningeal irritation occurs in many, varied clinical conditions and may be experimentally produced in animals. Inflammatory lesions of the meninges constitute the commonest cause. Among the more prevalent are tuberculosis, epidemic cerebrospinal meningitis, and pneumococcic, streptococcic and influenzal meningitis. Other inflammatory agents include virus infections (acute lymphocytic choriomeningitis, herpes zoster, acute anterior poliomyelitis and the encephalitides), yeast and fungous infections and syphilis.

Among the chemical agents which may provoke an irritative meningeal reaction is blood in the subarachnoid space. This is oftenest associated with other lesions, among which may be mentioned cranial trauma; aneurysms of various types; cerebrovascular disease, which may be associated with intracerebral bleeding; bleeding from intracranial or intraspinal tumors and varices, and bleeding which may inadvertently accompany cisternal, ventricular or lumbar puncture. Blood in the subarach-

2. Brudzinski, J.: Un signe nouveau sur les membres inférieures dans les meningites chez les enfants, *Arch. de med. d. enf.* **12**:745, 1909.

3. von Bikeles, G.: Bemerkung über ein Event. Analoges zum Kernigschen (und Lasqueschen), Phaenomen an den oberen Extremitäten, *Neurol. Centralbl.* **36**:407, 1917.

noid space is a particular offender and may produce exquisitely advanced degrees of meningeal irritation.

Among the provocative agents that may be introduced into the sub-arachnoid space from without the body are air or oxygen, iodized oils, penicillin and other antibiotics, anesthetics and proteins, such as those in antiserums or plasma and in the Swift-Ellis therapy.

Some curious and poorly understood cases of meningeal irritation occur with parameningeal diseases, in which the primary seat of disease is at a distance from the meninges. The most frequently encountered condition of this sort is apical or beginning central lobar pneumonia, in which the initial physical examination may reveal only fever, leukocytosis and meningeal signs. Meningism may also occur in typhoid and in the terminal stages of debilitating disease. More rarely, signs of meningeal irritation may be present in patients with pelvic inflammatory disease. They are said to occur in uremia, although I have never known this to happen.

Neoplastic diseases and some of the chronic granulomas may also be effective in producing meningeal irritation. These are relatively uncommon causes and include medulloblastoma, carcinomatosis and Hodgkin's disease.

#### MENINGEAL IRRITATION AND CONCOMITANT HEMIPARESIS

*Cranial Trauma.*—One of the most frequent clinical situations in which these two conditions may coexist is in injuries to the cranial contents.

*Case 27.*—E. G., a white man aged 47, was crossing the street against a traffic signal when he was struck by an automobile and thrown about 10 feet (3 meters). According to witnesses, he struck the pavement with the left side of his head and his left shoulder and lay there motionless. He was taken to a hospital, where he remained unconscious for three days.

The initial physical examination revealed the following neurologic status:

1. The patient was in deep coma. There were retraction of the head and a tendency to opisthotonos when he was lying on either side. 3. When the head was passively flexed on the chest, the right thigh flexed, but not the left. 4. When the left leg was raised in testing for the meningeal leg signs, the right thigh flexed in response. When the right leg was similarly raised, there was no response of the left thigh. 5. The meningeal arm signs were not present. 6. The tendon reflexes were barely obtainable on either side, and there were no pathologic superficial reflexes, such as the Babinski sign. 7. Motor power, coordination and sensation could not be tested at this time.

Spinal puncture revealed a resting spinal fluid pressure of 150 mm. of water. The Queckenstedt test was not made. The fluid was grossly bloody and contained 90,000 red blood cells per cubic millimeter. Roentgenographic studies of the skull revealed nothing unusual.

Examination two days later revealed diminution in the intensity of the meningeal signs, particularly in retraction of the head. The left thigh still did not flex when an attempt was made to elicit the meningeal signs. The tendon reflexes had become more active and were stronger on the left than on the right. At this time it was questionable whether the Babinski sign was obtainable on the

left. The patient was stuporous but could be partially aroused at times. At this stage there were 10,000 red blood cells per cubic millimeter in the spinal fluid.

Four days after admission the patient was fully conscious. The meningeal signs were slight, but there was still no reflex flexion of the left thigh when they were elicited. A striking difference was apparent between the very active tendon reflexes on the left side and the normal tendon reflexes on the right. A typical Babinski response to plantar stimulation occurred on the left side, and the muscle groups of the left arm and leg were noticeably weak. There was also weakness of the left side of the face of central type. Sensory signs were present. A slight intention tremor appeared on the left side in the finger to nose test.

*Comment.*—This patient suffered a traumatic cerebral lesion associated with subarchnoid hemorrhage. The lesion involved the right cerebral hemisphere by contrecoup and gave rise to left hemiparesis, as the pyramidal tract signs showed, when the patient recovered consciousness. The earliest clinical sign pointing to the hemiparesis appeared to be the failure of the left thigh to flex when the meningeal signs were elicited at the time of the initial examination. This lateralizing modification of the flexor responses in the presence of meningeal irritation appeared to be independent of the state of consciousness or the state of concussion.

*Suppurative Intracranial Complications of Infections of the Ear and Sinuses.*—Such complications may be accompanied with meningeal irritation, as well as localized lesions of the cerebral hemispheres.

*Case 32.*—A. G., a white man aged 32, had usually been in vigorous good health. While at the home of a physician friend of his, he complained of headache and stiffness of the neck. He was advised to go to bed. The next day he had a feeling of general malaise, and the headache was more constant. He had a temperature of 100.6 F., some retraction of the head and stiffness of the neck. Passive flexion of the head was followed by bilateral flexion of the thigh, and passive leg raising on either side resulted in ipsilateral contraction of the hamstring muscles with flexion of the contralateral thigh. There was no muscular weakness. Sensation was intact; the tendon and superficial reflexes were normal, and coordination was unimpaired. The cranial nerves were normal. The spinal fluid was under a pressure of 200 mm. of water and contained 950 cells per cubic millimeter, 85 per cent of which were polymorphonuclear in type. No organisms were observed on direct smear or culture. Although the patient had a history of disease of the paranasal sinuses, the sinuses and ears appeared clinically normal to direct and roentgenographic inspection at this time. No pulmonary disease was present.

The patient was given sulfadiazine by mouth, and the blood level of the drug was brought to 9.5 mg. per hundred cubic centimeters in three days. He was also given 2,000 units of penicillin three times daily by intrathecal injection the first day and 4,000 units thereafter. At the end of five days his condition showed no improvement and he was becoming stuporous. The intensity of the meningeal signs at this time was undiminished except that the right thigh did not flex either on raising the leg or on flexing the neck. The rest of the neurologic status was normal. The spinal fluid was sterile and contained 500 cells per cubic millimeter, 98 per cent of which were polymorphonuclear cells.

The stupor passed into coma on the sixth day. There was still absence of flexion of the right thigh when the meningeal signs were elicited. Both optic disks at this time showed slight edema. The tendon reflexes were generally less active,

and the Babinski sign was not elicited. It was reasoned that the therapy the patient was receiving would have been sufficient had it not been either that the responsible organism was resistant to both penicillin and sulfadiazine or that a continuous reinfection from a suppurative focus existed. That this focus was probably in the brain was indicated by the papilledema and the deepening coma. That it might be in the left cerebral hemisphere was indicated by the failure of the right thigh to flex when an attempt was made to elicit the meningeal signs.

On the seventh day the papilledema had increased and the coma deepened. The meningeal signs persisted except that the right thigh did not flex. A ventriculogram showed a decided shift of the ventricular system to the right and posterior displacement of the left lateral ventricle. The diagnosis of a mass lesion in the frontal pole of the left cerebral hemisphere was made, and a trephine opening was made above the left frontal sinus enabled the neurosurgeon to place a drain in the cavity of a superficial abscess in the frontal pole.

After fourteen days of a comparatively uneventful postoperative convalescence, the temperature again rose to 101 F. The neck was rigid, and, again, there was no flexion of the right thigh when the neck was flexed or when the left leg was used in testing for the Kernig or the Brudzinski sign. There was palsy of the right side of the face of central type, but no other muscular weakness. The tendon reflexes of the right leg were slightly increased, and the Babinski sign was not elicited. Penicillin given intramuscularly and intrathecally cleared the spinal fluid of cells and eliminated the signs of meningeal irritation. The patient recovered steadily thereafter. In two months the only residual neurologic signs were witzelsucht and palsy of the right side of the face of central type.

*Comment.*—In this case the illness probably began with the formation of an abscess in the frontal lobe. This abscess drained into the subarachnoid space, giving the clinical appearance and physical signs of meningitis. The failure of the right thigh to flex when the meningeal signs were elicited was the earliest physical evidence lateralizing the lesion to the left cerebral hemisphere. Once, after the abscess had been tapped, there was spread of infected material into the subarachnoid space, and again a full set of meningeal signs appeared except for flexion of the thigh contralateral to the hemispheric lesion.

*Intracerebral Hemorrhage with Leakage of Blood into the Subarachnoid Space.*—In this condition both meningeal signs and hemiparesis may occur.

*Case 1.*—C. W., a white woman aged 64, was treated by her family physician for hypertension, which was known to have existed for five years. Her heart was moderately enlarged, but she had no history of cardiac or renal failure. She complained of headaches, which were chiefly occipital and frontal, and which lasted one or two days. They came on at irregular intervals and were not relieved by coal tar analgesics. For the past year and a half she had been given potassium thiocyanate N.F., the blood level of the drug varying from 4.0 to 8.0 mg. per hundred cubic centimeters. During the past two years her blood pressure readings had ranged from 220 to 180 systolic and 120 to 100 diastolic, and they had not been significantly altered by the thiocyanate therapy; but both the patient and her physician stated that she had fewer headaches and felt less tense while taking the thiocyanate.

One evening, while sitting, she slumped and could not be roused. While still unconscious and limp, she was taken to the hospital, where she remained comatose for three days. In addition to the physical evidence of hypertensive cardiovascular disease, she had retraction of the head, slight arching of the back, almost complete absence of tendon reflexes and equally contracted pupils (she had been given morphine before admission). Passive flexion of the head on the chest met with resistance of the extensor muscles of the neck and flexion of the left thigh. Extension of the right leg and thigh in either the Kernig or the Brudzinski maneuver was followed by flexion of the left thigh on the abdomen. No responsive motion of the right thigh could be elicited on executing these passive movements of the left leg. Her coma precluded sensory or motor testing at this time. There were no pathologic superficial reflexes. Cell counts of the spinal fluid revealed 100,000 red blood cells per cubic millimeter the first day, 75,000 the second day and 10,000 the fourth day.

On the third day the patient began to show signs of returning consciousness. With increasing restlessness, it soon became apparent that she had pronounced weakness of the right arm and leg. The general meningeal signs were still present except for flexion of the right thigh on stimulation either of the neck or of the left leg. The patient was also aphasic. A Babinski sign was elicited on the right side. There were no sensory signs. The patient recovered rapidly from the signs and symptoms of the meningeal irritation and the spinal fluid became free of blood cells, but the right hemiparesis and the aphasia never completely disappeared.

*Comment.*—This case appeared to be one of an intracerebral hemorrhage in the left cerebral hemisphere with leakage of blood into the subarachnoid space. The coma, absence of movement of the limbs on either side, decreased activity of tendon reflexes and absence of pathologic reflexes gave no clue in the early stages of this patient's illness that a hemiparetic syndrome was present in addition to the meningeal irritation. The earliest sign pointing to the existence of the right hemiparesis was the failure of flexion of the right thigh when the neck and leg signs of meningeal irritation were elicited.

*Intracranial Aneurysms.*—Depending on their position and state intracranial aneurysms may give rise to both hemiparesis and subarachnoid hemorrhage.

*Case 4.*—A. W., a woman aged 46, a school teacher, was brought into the hospital in coma, with a history of having suffered from intense headaches at rare intervals. She usually had to go to bed for several days when these attacks appeared, and no medication or other treatment she had received from time to time had ever completely relieved her of the intense, generalized pain. Between these attacks she felt perfectly well and was a happy, alert, well adjusted woman. One day before the present admission to the hospital a headache began and, as usual, became rapidly worse. Within two hours she was in acute delirium, and within three hours she was in coma.

The initial examination revealed an increase in temperature (101.2 F.), stiffness of the neck, flexion of the right thigh on bending the neck and on raising the left leg but no flexion of the left thigh when meningeal signs were elicited. Her lids were semiclosed, and the right pupil was a trifle larger than the left. There was generalized reduction in activity of the tendon reflexes; no pathologic reflex was present. With the patient recumbent, the spinal fluid had an initial pressure

of 230 mm. of water and was grossly bloody. It contained 200,000 red blood cells per cubic millimeter. Although the prothrombin time was normal, the patient was given a preparation of vitamin K intravenously every six hours. There was little change over a period of three days, and at the end of this time the spinal fluid still contained 180,000 red blood cells per cubic millimeter. The most probable diagnosis was that of bleeding intracranial aneurysm. On the basis of the failure of the left thigh to flex on elicitation of meningeal signs, it was thought that the aneurysm was on the right side of the brain, rather than on the left. The persistently large size of the right pupil also suggested this lateralization. These two signs suggested a localization in the anterior portion of the circle of Willis on the right side. No bruit was heard over the skull or the eyes.

On the fourth day in the hospital the right internal carotid artery was exposed and a linen tape placed around the artery; the untied ends of the tape were then brought to the surface. The two ends of the untied tape were raised for thirty seconds at a time every ten minutes for the first six hours and then every five minutes for the next twelve hours. Ten hours after the operation the patient moved for the first time since admission. These movements were of all four extremities but were more frequent in the right arm and leg than in the left. At this time the patient was observed to have ptosis of the right lid and paralysis of movement of the right eye in every direction except to the temporal side. The tape was then raised for thirty seconds of every two minutes. During the next thirty-six hours she regained consciousness, and the red cell count of the spinal fluid dropped to 52,000 per cubic millimeter. After her return to consciousness the ptosis of the right lid was extreme, and the paralysis of the right eye was complete except for outward rotation. The tendon reflexes were increased and a Babinski sign was elicited on the left side, and slight, but definite, weakness of the lower portion of the left side of the face and the left arm and leg was noted. With increasing compression of the right carotid artery, none of these hemiparetic signs became worse, and the patient's headache was less painful during this procedure. These observations, and the fact that the patient was right handed, prompted a decision to ligate the right carotid artery permanently. This operation was carried out on the tenth day of hospitalization. Thereafter, both the headache and the manifestations of meningeal irritation subsided, and the patient left the hospital with almost complete paralysis of the right oculomotor nerve and mild left hemiparesis.

Within two months, there was almost no evidence of the hemiparesis, and paralysis of the right oculomotor nerve was less complete.

*Comment.*—The patient had a history of recurrent severe headache, which probably represented multiple episodes of bleeding from an intracranial aneurysm in the anterior portion of the circle of Willis on the right. When the patient was seen for the first time, the only clue to laterality was the failure of the left thigh to flex in tests for the meningeal signs. This observation was in accord with the presence of a larger pupil on the right. The subarachnoid hemorrhage showed no sign of clearing, and the open type of intermittent carotid compression was used on the right side. The lateralization of the lesion was indicated by the absence of flexion of the left thigh as a modification of the meningeal signs. The subsequent course after complete ligation was in consonance with the diagnosis.

*Data on 47 Cases of Concurrent Meningeal Irritation and Hemiparesis.*

Case	Age, Yr.	Sex	Side of Hemiparesis	Disease	Degree of Meningeal Signs, 1 to 4 plus	Coma, 0 to 4 plus	Modification*	
							Neck	Sound leg
1	64	F	R	Cerebrovascular disease	1+	4+	+	+
2	75	F	L	Cerebrovascular disease	2+	—	+	—
3	47	F	L	Cerebrovascular disease	4+	2+	+	+
4	52	M	R	Cerebrovascular disease	4+	1+	+	+
5	60	F	L	Cerebrovascular disease	2+	4+	—	—
6	52	M	R	Cerebrovascular disease	3+	2+	+	+
7	72	M	R	Cerebrovascular disease	3+	1+	+	+
8	48	M	L	Cerebrovascular disease	2+	3+	+	+
9	39	F	R	Cerebrovascular disease	4+	2+	—	+
10	59	M	R	Cerebrovascular disease	1+	4+	—	—
11	58	M	R	Cerebrovascular disease	3+	1+	—	+
12	4	F	L	Meningeal and cerebral infection	4+	4+	+	+
13	32	M	R	Meningeal and cerebral infection	4+	—	+	—
14	23	M	L	Meningeal and cerebral infection	1+	3+	+	+
15	29	F	R	Meningeal and cerebral infection	3+	2+	+	+
16	46	F	L	Meningeal and cerebral infection	4+	—	—	+
17	½	F	L	Meningeal and cerebral infection	1+	4+	+	+
18	12	F	R	Meningeal and cerebral infection	3+	2+	+	+
19	39	M	R	Meningeal and cerebral infection	2+	3+	—	+
20	17	M	R	Meningeal and cerebral infection	2+	4+	—	+
21	29	F	R	Meningeal and cerebral infection	1+	3+	—	+
22	60	M	L	Meningeal and cerebral infection	4+	—	+	+
23	6	M	L	Cerebral trauma	4+	4+	+	+
24	40	F	L	Cerebral trauma	2+	3+	+	+
25	21	F	R	Cerebral trauma	2+	2+	+	+
26	23	F	L	Cerebral trauma	3+	2+	—	+
27	47	M	R	Cerebral trauma	1+	3+	+	—
28	27	M	R	Cerebral trauma	3+	4+	+	+
29	64	M	R	Cerebral trauma	2+	4+	+	+
30	38	M	R	Cerebral trauma	3+	1+	+	+
31	70	F	R	Cerebral trauma	2+	4+	+	+
32	16	M	L	Cerebral trauma	4+	1+	+	+
33	25	M	R	Cerebral trauma	3+	1+	+	—
34	32	F	L	Cerebral trauma	2+	3+	+	+
35	39	M	L	Cerebral trauma	3+	4+	+	+
36	38	M	L	Cerebral trauma	3+	1+	+	+
37	12	F	R	Cerebral trauma	4+	2+	+	+
38	4	F	L	Cerebral trauma	4+	3+	+	+

*Other Cases of Concurrent Meningeal Irritation.*—Since becoming interested in this modification of the meningeal signs, I have accumulated 47 cases in which there were concurrent meningeal irritation and hemiparesis. The data in these cases are presented in the accompanying table.

*Data on 47 cases of concurrent meningeal irritation and hemiparesis (con't.)*

Case	Age, Yr.	Sex	Side of Hemiparesis	Disease	Degree of Meningeal Signs, 1 to 4 plus	Coma, 0 to 4 plus	Modification*	
							Neck	Sound leg
39	62	F	R	Cerebral trauma	4+	1+	—	+
40	46	F	L	Bleeding aneurysm	2+	4+	+	+
41	39	M	R	Bleeding aneurysm	3+	—	+	+
42	22	F	R	Bleeding aneurysm	4+	—	+	+
43	34	M	L	Bleeding aneurysm	4+	1+	—	+
44	37	M	L	Bleeding aneurysm	2+	—	+	+
45	36	M	L	Iodized oil and spinal cord tumor	4+	—	+	+
46	29	M	R	Encephalogram and cerebral tumor	3+	—	+	+
47	46	F	R	Encephalogram and cerebral tumor	2+	—	+	+

\*The presence of the modification is indicated by +; its questionable presence or absence by —.

All the cases tabulated were selected because unmistakable signs both of meningeal irritation and of hemiparesis were present, although more customary evidence of the latter sometimes did not immediately appear but was obtained as the meningeal irritation subsided. The modification of the meningeal signs in which the hemiparetic thigh does not flex showed a remarkable constancy in these cases, and the sign has not been found misleading in any other case. In cases in which the coma was most intense and the meningeal signs were slight, the modification tended to be absent or less obvious.

#### NEUROPHYSIOLOGIC BASIS OF THE MENINGEAL SIGNS AND THE MODIFICATION INTRODUCED BY HEMIPARESIS

Remarkably little basic information is available as to the pathways and mechanisms utilized in the production of meningeal signs. These signs are often regarded as exaggerated flexor responses, and the essential pathologic lesion appears to be in the portion of the meninges at the base of the brain. Fulton<sup>4</sup> reported that tugging at the basal meninges in the experimental animal is capable of producing meningeal signs, and there is a positive correlation between the intensity of basal meningitis and that of meningeal signs. Another favorite explanation of the mechanism of the

4. Fulton, J. F. *Physiology of the Nervous System*, New York, Oxford University Press, 1938, p. 97.

meningeal signs is that they depend on irritation of the thoracic spinal nerve roots. Presumably, this would mean that flexor responses are exaggerated because of this constant stimulus. This assumption has some pathologic justification in that the meningeal recesses about the thoracic nerve roots are oftenest involved in the meningeal inflammation. An explanation often advanced for the leg signs is that the sciatic nerve is stretched and, because the roots have been irritated, there is reflex contraction of the biceps femoris muscle. This explanation is insufficient to account for the flexion of the contralateral thigh and does not apply at all to the reflexes elicited by passive flexion of the neck. The whole problem would be simple were it not that both passive flexion of the head on the chest and leg raising are capable of producing in the thigh the clinical signs of meningeal irritation.

With concurrent meningeal irritation and hemiparesis, the hemiparetic thigh usually does not flex on either neck or leg stimulation. This is so whether or not signs of sensory defect are present. Therefore, one of the necessary pathways for the leg response is in the pyramidal pathways which supply the lumbar portion of the cord. The explanation that a stretched sciatic nerve causes a local reflex with contralateral components is obviously insufficient to explain why the hemiparetic thigh fails to flex when the sciatic nerve of the sound leg is stretched. The lower part of the spinal cord is not itself involved in a local lesion. In the case of neck stimulation and failure of the paretic thigh to flex, the case for the pyramidal tract as a necessary pathway is even stronger, since all other factors act as controls between the sound and the hemiparetic side.

The exact relation of the tonic neck reflexes to the meningeal signs is still open to question. The neck reflexes are, of course, best elicited in the decerebrate human subject or the laboratory animal. The afferent limb of the reflex arc extends almost certainly from the neck muscles through the cervical roots of the upper segments of the spinal cord. There is no available evidence to suggest that the preparation with high bilateral section of the pyramidal tract, which is most suitable for the demonstration of tonic neck reflexes, bears any important relation to the cases of unilateral pyramidal tract disease with meningeal irritation cited here. Further, the thigh segment of the response to ventroflexion of the head in the decerebrate animal is either extension or relaxation of the lower extremities, but in no case flexion. Therefore the phenomena of the tonic neck reflex cannot constitute a valid argument against the necessity for an intact pyramidal tract in order that the thigh flexion segment of the meningeal signs may appear.

While the rest of the necessary pathways and mechanisms is open to doubt, there is clinical evidence that intact pyramidal pathways are necessary for the appearance of the thigh flexion response of the menin-

geal signs. The local spinal cord reflexes are not sufficient in the case of stimulation of the contralateral leg to explain failure of flexion of the hemiparetic thigh in cases of meningeal irritation, as these are usually intact. In the case of the neck flexion test in patients with concomitant meningeal irritation and hemiparesis due to cerebral lesions, the failure of the hemiparetic thigh to flex is so constantly present that little doubt can be entertained that the intact pyramidal tract is one of the necessary pathways for the thigh flexion segment of the meningeal signs.

#### PRACTICAL USE OF THE MODIFICATION

Since failure of the hemiparetic thigh to flex occurs in the presence of meningeal irritation and hemiparesis, the clinician faced by a comatose patient with meningeal irritation may often gain early evidence as to whether hemiparesis is present and, if so, on which side. In the conscious patient the modification may be an additional interesting, although unnecessary, sign. In the presence of coma it has often been useful in cases of cranial trauma, the cerebral neoplastic diseases, suppurative infection and aneurysm. In cases of hypertensive and other cerebrovascular disease this additional information is seldom the basis for any practical therapy. The modification is often present at a time when no other hemiparetic signs can be elicited.

#### SUMMARY

In the majority of cases of meningeal irritation meningeal signs are present.

With concomitant hemiparesis the signs are modified; in most instances there is absence of flexion of the thigh on the abdomen on the hemiparetic side.

The neurophysiologic implications of this modification of the meningeal signs are discussed. An intact pyramidal tract is considered necessary for flexion of the thigh as part of the meningeal signs.

Application of this knowledge in cases of comatose patients with cranial trauma, cerebral neoplasm and aneurysms is indicated.

106 Broadway.

## EFFECT OF OPTIC AND ACOUSTIC STIMULI ON THE CORTEX AND HYPOTHALAMUS UNDER CONDITIONS OF Picrotoxin Convulsions

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THE INFLUENCE of afferent impulses elicited by stimulation of the sciatic nerve and of the posterior portion of the hypothalamus was the subject of a previous investigation.<sup>1</sup> It was found that these factors induce and intensify convulsive movements and greatly alter cortical activity. Examples of intensification, as well as of suppression, of convulsant potentials as the result of such stimuli were presented, and the mechanism of the underlying neurophysiologic processes was discussed. The present investigation is concerned with the influence of sensory impulses (optic and acoustic) in similar circumstances. This effect is obviously related to clinical problems of epilepsy, since a sensory "aura" frequently precedes the motor attack, and "acoustico-motor" (Penfield<sup>2</sup>) and "musicogenic" forms of epilepsy (Critchley<sup>3</sup>) have been described in the literature.

### METHOD

The procedure was similar to that used in the preceding investigation.<sup>1</sup> Cats were anesthetized with diallylbarbituric acid with urethane ("dial with urethane") before and after intravenous injection of picrotoxin. Various acoustic stimuli were studied in their effect on the primary acoustic projection area. In another series, a light was focused on the atropinized pupil, and its effect on the optic projection area was recorded. These experiments were performed at different degrees of picrotoxinization, and the effect was noted on specific projection, as well as on other cortical, areas.

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1. Gellhorn, E., and Ballin, H. M.: Role of Afferent Impulses in Experimental Convulsions, *Arch. Neurol. Psychiat.*, to be published.

2. Penfield, W., and Erickson, T. C.: *Epilepsy and Cerebral Localization*, Springfield, Ill., Charles C Thomas, Publisher, 1941.

3. Critchley, M.: Musicogenic Epilepsy, *Brain* **60**:13-27, 1937.

## RESULTS

*Influence of Optic Stimuli on Cortical and Hypothalamic Potentials at Various Stages of Picrotoxin Poisoning.*—As noted by previous investigators (Kornmüller<sup>4</sup>, Fischer and Lowenbach<sup>5</sup>), the optic cortical response increases under the influence of convulsive drugs. These changes

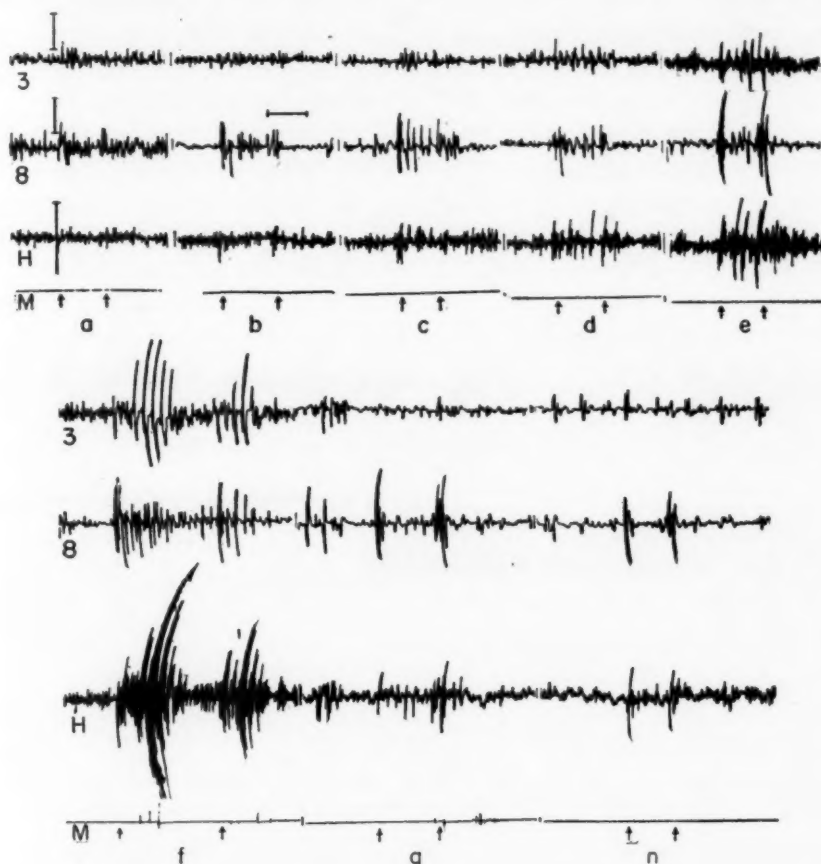


Fig. 1.—Effect of optic stimulation (indicated by two arrows) on cortex and hypothalamus at different stages of picrotoxinization. 3 indicates motor area (cruciate sulcus); 8, optic projection area; H, posterior portion of hypothalamus; M, movements, partially suppressed by "intocostrin." The cat was anesthetized with diallylbarbituric acid ("dial") with urethane. The amount of picrotoxin injected intravenously, and the time intervals of the recordings are indicated as follows: (a) zero minutes, 0.2 mg. per kilogram of body weight; (b) twenty-seven minutes, 0.1 mg. per kilogram; (c) forty-one minutes, 0.2 mg. per kilogram; (d) fifty-one minutes; (e) sixty minutes, 0.1 mg. per kilogram; (f) sixty-one minutes; (g) seventy-one minutes; (h) eighty-one minutes.

4. Kornmüller, A. E.: Die bioelektrischen Erscheinungen der Hirnrindengebiete, Leipzig, Georg Thieme, 1937.

5. Fischer, M. H., and Löwenbach, H.: Aktionsströme des Zentralnervensystems unter der Einwirkung von Krampfgiften, Arch. f. exper. Path. u. Pharmacol. 174:357-382 and 502-516, 1934.

may be considerable and still be restricted to the specific projection area. If, however, picrotoxinization is carried further, an optic response may appear outside the optic cortex. This is well illustrated in figure 1, in which by recording potentials in the optic projection area, the motor cortex and the hypothalamus, the effect of optic stimuli is tested at progressing degrees of convulsive activity. At first (*a*) a slight, but distinct, response occurs in the optic area only, the action of the stimulus being restricted to an on and off effect. As the picrotoxin poisoning increases, the response is qualitatively and quantitatively altered and becomes more widespread, affecting cortical and subcortical areas previously not altered under conditions of optic stimulation. The electrocorticogram of the optic area reveals that the on and off response not only increases in amplitude but appears in the form of repetitive discharges. While the retina is exposed to light, the potentials are also increased in

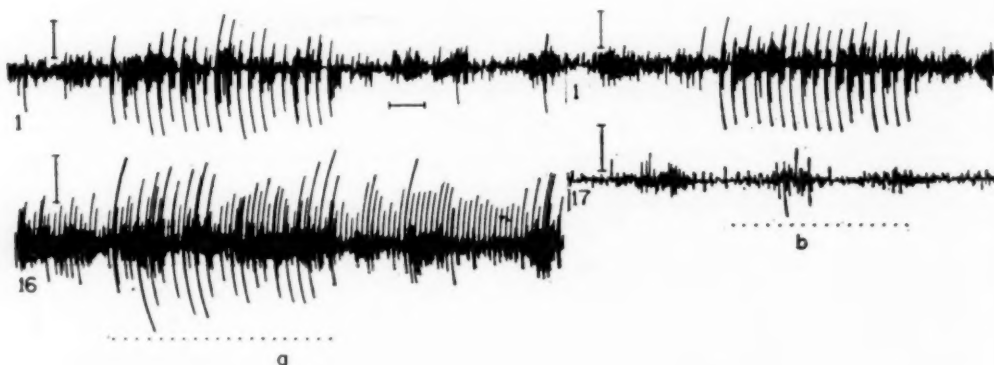


Fig. 2.—Effect of acoustic stimulation on the acoustic projection area (1), on the anterior third of the gyrus marginalis (16) and on the motor area (17) in a picrotoxinized cat. Acoustic stimulation is indicated by the dotted line.

amplitude, as figure 1 *b* to *e* indicates, but the main effect appears as an increased and prolonged on and off effect.

The electrograms of the hypothalamus and of the motor cortex show more striking changes. No optic response was recorded from these structures under control conditions, whereas under the influence of picrotoxin they showed pronounced on and off responses, the repetitive character of which was clearly evident. This record was taken from a partially curarized cat; movements which were recorded in the bottom line of figure 1 appeared only with increased degrees of picrotoxinization. It is noted that at the peak of convulsive activity (fig. 1*f*), the on and off effects are accompanied with convulsive movements. These effects, as well as the action on various cortical areas and on the hypothalamus, are reversible (*g,h*).

*Action of Acoustic Stimulation on the Cortex During Picrotoxin Convulsions.*—Similar experiments performed with an acoustic stimulus showed that the amplitude of the action potentials, indicating the response to auditory impulses, increased in the acoustic cortical area with increasing degrees of picrotoxin poisoning. A spread of this response to

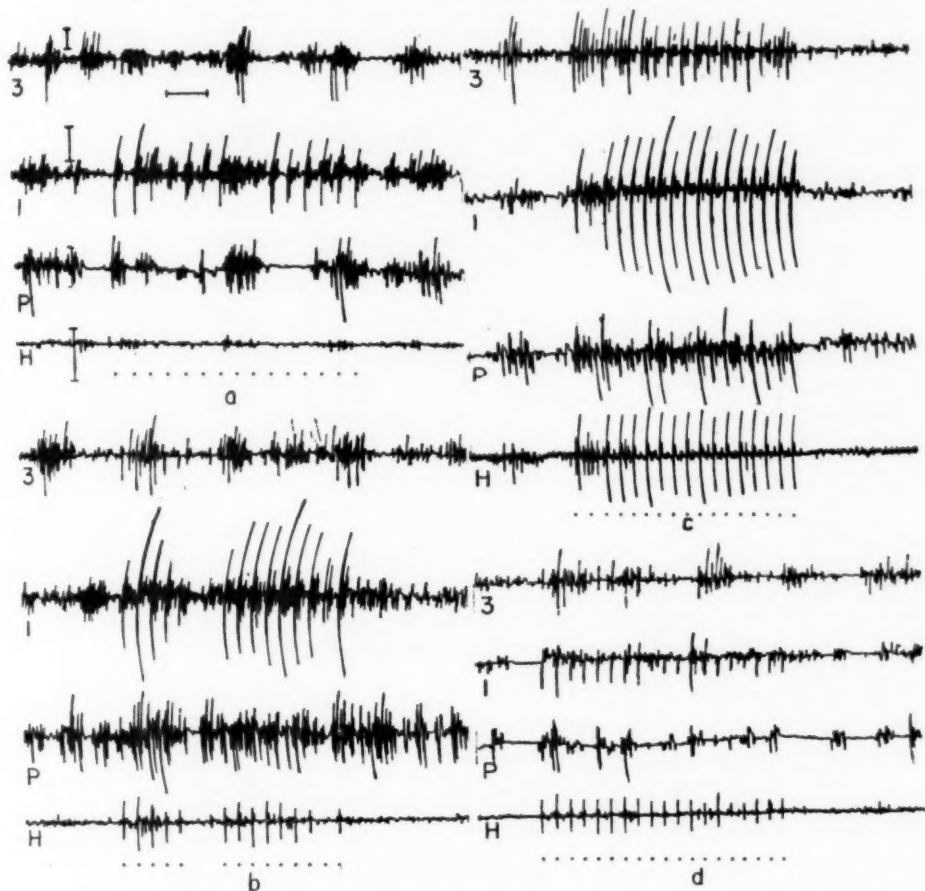


Fig. 3.—Effect of acoustic stimulation on the motor area (3), the acoustic projection area (1), the posterior (occipital) suppressor area (P) and the posterior portion of the hypothalamus (H) at various degrees of convulsive activity induced by intravenous injection of picrotoxin (0.7 mg. per kilogram) between 0 and fifty minutes after injection. (a) represents 0 minutes; (b) thirty-one minutes; (c) seventy-one minutes; (d) ninety-five minutes.

other areas is illustrated in figure 2, in which, at a certain degree of picrotoxinization, a distinct acoustic response also appears in or near the optic projection area, while the motor cortex is still unresponsive. Figure 3 permits one to compare the reactivity of various cortical areas and the hypothalamus under conditions of increasing convulsive activity. Whereas under control conditions and at initial stages of picrotoxin poisoning only the acoustic area reacts, at a final stage, represented by figure 3c,

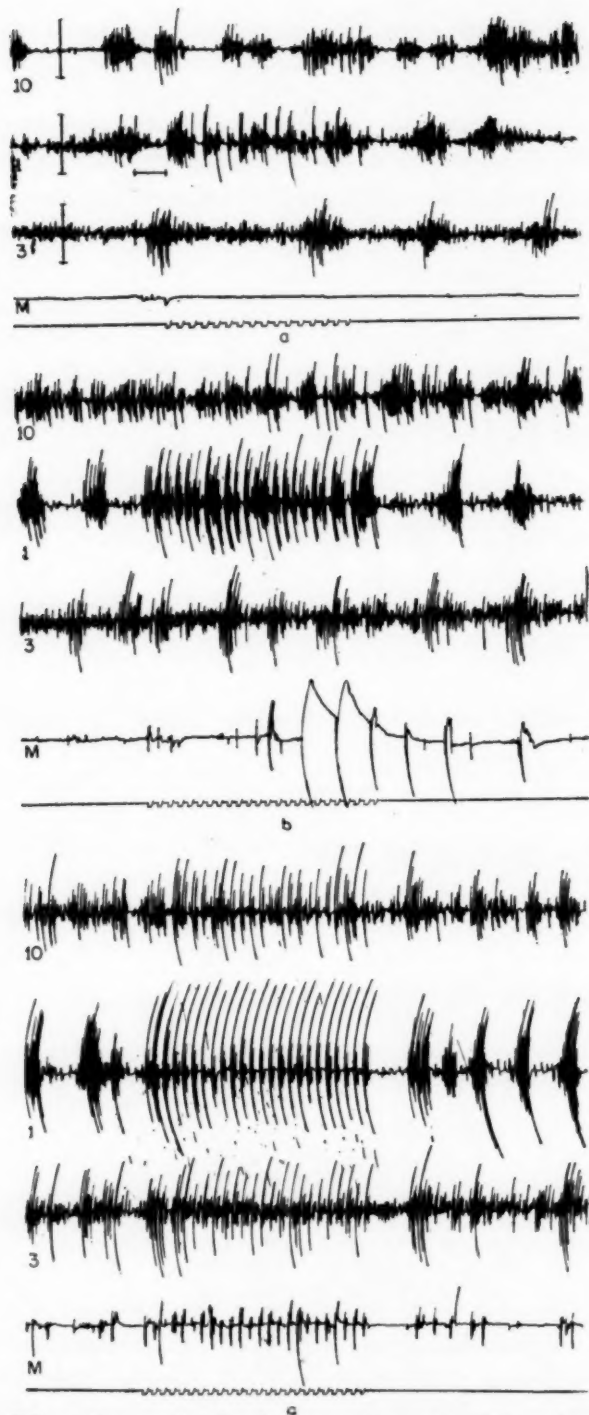


Fig. 4.—Effect of acoustic stimulation on the optic (10) and on the auditory (1) projection areas and the motor area (3) under conditions of increased picrotoxinization induced by gradual injection intravenously of 0.9 mg. of picrotoxin per kilogram of body weight. The fourth line indicates the movements of the extremities; the last line, the time of acoustic stimulation.

various nonacoustic cortical areas, as well as the hypothalamus, show distinct reactions to each stimulus. It is interesting to note that the occipital suppressor area participates likewise in this phenomenon as the picrotoxinization increases. Figure 3 shows also that during the earlier stages of picrotoxin poisoning the acoustic response outside the acoustic projection area appears first in the hypothalamus and later in the non-acoustic cortical areas. Similarly, it is seen in figure 3*d* that as the picrotoxin intoxication recedes the response to acoustic stimulation persists in the hypothalamus (and, of course, in the acoustic cortical projection area) at a time when it has disappeared in nonacoustic cortical areas.

It was shown in an earlier paper that afferent stimuli elicited by electrical or mechanical stimulation of the sciatic nerve or by electrical stimulation of the posterior portion of the hypothalamus may precipitate or aggravate convulsions in a picrotoxinized cat. Therefore the question arose whether auditory or optic stimuli may cause similar effects. Figure 4 illustrates an experiment in which potentials from several cortical areas and movements were recorded with the crystograph. At an earlier stage of picrotoxinization (*a*), the acoustic response was restricted to the auditory projection area, and motor phenomena were absent. At a later stage (*b*) only traces of movements were recorded prior to auditory stimulation, but the latter evoked movements which greatly increased in intensity. At a final stage (*c*) moderate convulsive movements, appearing at irregular intervals, were recorded prior to auditory stimulation. The acoustic stimuli regularized these responses, since each of them caused a distinct motor action. A similar effect as a result of optic stimulation is seen in figure 1. However, generalized convulsions, such as were frequently elicited by sciatic or hypothalamic stimulation in the picrotoxinized cat, were not produced by optic or acoustic stimulation, with the possible exception of a single experiment.

#### COMMENT

The present experiments have shown that under the influence of picrotoxin afferent impulses originating in the retina or in the organ of Corti not only produce increased responses (Kornmüller,<sup>4</sup> Fischer and Löwenbach,<sup>5</sup> Bremer<sup>6</sup>) in their respective projection areas but may extend these effects to nonspecific areas as well. In general, with the possible exception of a single experiment, these stimuli fail to produce generalized convulsions. The convulsive responses elicited by optic or acoustic stimuli were restricted to the time of application of these stimuli. This statement applies for the motor phenomena (overt convulsive movements), as well as for the change in cortical potentials.

6. Bremer, F.: Etude oscillographique des réponses sensorielles de l'aire acoustique corticale chez le chat, *Arch. internat. de physiol.* **53**:53-103, 1943.

Fischer and Löwenbach<sup>5</sup> and Gozzano<sup>7</sup> noted that after local application of strychnine to the area striata repeated optic stimuli may elicit a convulsive attack which outlasts the period of stimulation. We failed to see such effects in picrotoxinized cats. The difference in the results of these authors and our own seems to be due to the fact that local application of strychnine permits one to perform experiments on a higher degree of convulsive activity than appears to be feasible when the convulsant drug is injected intravenously. Obviously, the spread of convulsive activity from specific projection areas to other cortical fields as a result of specific afferent impulses, which was the chief objective of this investigation, can be studied only if the cortex is in a relatively light convulsive or subconvulsive state. This was accomplished in the present work by the intravenous administration of suitable quantities of picrotoxin.

The observation of Ades<sup>8</sup> that local strychninization of the primary acoustic projection area leads to the firing of an adjacent secondary acoustic area is related to the present study. However, in our own experience, subconvulsant doses of picrotoxin permit one to evoke responses to an acoustic stimulus in a much wider cortical area, and similar results were obtained with optic stimuli. This larger area is functionally unrelated to the specific projection area.

Kornmüller<sup>4</sup> observed also that convulsive discharges elicited by the application of convulsant drugs to the area striata were not accompanied with general convulsions. This statement can now be amplified. Apparently, convulsive discharges may appear in picrotoxinized cats in wide cortical areas, particularly under the influence of optic or acoustic stimuli, without producing overt convulsions. Similar observations were reported in the preceding paper, in which the effect of hypothalamic and sciatic stimulation on convulsive potentials and movements were studied. Whether this peculiar effect is typical for picrotoxin or applies to other convulsant drugs as well is under investigation.

#### SUMMARY

The effect of optic and acoustic stimulation on cortical potentials and movements was investigated under the influence of increasing degrees of picrotoxin poisoning. The results were as follows:

With progressing degrees of intoxication, the sensory response elicited in the specific cortical projection areas increased in amplitude and also

7. Gozzano, M.: Bioelektrische Erscheinungen bei der Reflexepilepsie, *J. f. Psychol. u. Neurol.* **47**:24-39, 1936.

8. Ades, H. W.: A Secondary Acoustic Area in the Cerebral Cortex of the Cat, *J. Neurophysiol.* **6**:59-64, 1943.

became repetitive. Moreover, sensory responses similar in quality and quantity appeared in previously nonresponding cortical areas (including the suppressor areas) and in the hypothalamus. The motor cortex was not particularly sensitive to picrotoxin discharges, since responses to an acoustic stimulus appeared in nonacoustic projection areas while they were absent in the motor cortex. Optic or acoustic stimuli may elicit or intensify convulsive movements, but these reactions were mostly confined to the moment of stimulation. Generalized convulsive movements were not induced with these stimuli.

## STURGE-WEBER SYNDROME

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IN RECENT years a number of reports have appeared of a condition variously designated as the Sturge-Weber syndrome, Kalischer-Dimitri disease or Brushfield-Wyatt disease. All these terms apparently refer to the same clinical entity. The condition is one of associated facial nevus with homolateral glaucoma and an intracranial pathologic process in the form of angiomatous changes, sometimes in the pia mater and at others in the cerebral cortex itself. As a rule calcium deposits of one type or another are seen. The pathologic changes in the brain are usually manifested by epileptic seizures, feeble-mindedness or visual field defects, the last-mentioned symptoms appearing when the occipital lobes are involved, as its often the case. Nussey and Miller<sup>1</sup> stated that it was Schirmer<sup>2</sup> in 1860, who first described a patient displaying an associated facial nevus and glaucoma. A few years later, in 1870, Sturge<sup>3</sup> recorded a case of nevus of the right side of the face, with right buphthalmos and epileptic fits of a jacksonian nature involving the left hand. Then Kalischer<sup>4</sup> published the first necropsy observations on such a condition in 1897, and finally in 1922, Weber<sup>5</sup> reported a case with calcifications of the brain on the same side as that of the facial nevus. Greenwald and Koota,<sup>6</sup> in

From the Mercy Hospital-Loyola University Clinics.

1. Nussey, A. M., and Miller, H. H.: Sturge's Disease, *Brit. M. J.* **1**:822-823, 1939.
2. Schirmer, R.: Ein Fall von Telangiectasie, *Arch. f. Ophth.* **7**:119-121, 1860.
3. Sturge, W. A.: A Case of Partial Epilepsy, Apparently Due to a Lesion of One of the Vaso-motor Centers of the Brain, *Tr. Clin. Soc. London* **12**:152-167, 1879.
4. Kalischer, S.: Demonstration des Gehirns eines Kindes mit Telangiectasie der linksseitigen Gesichts-Kopfhaut und Hirnoberfläche, *klin. Wehnschr.* **43**:1059, 1897.
5. Weber, F. P.: Right-Sided Hemi-Hypertrophy Resulting from Right-Sided Congenital Spastic Hemiplegia, with a Morbid Condition of the Left Side of the Brain Revealed by Radiograms, *J. Neurol. & Psychopath.* **3**:134-139, 1922.
6. Greenwald, H. J. and Koota, J.: Associated Facial and Intracranial Hemangiomas, *Am. J. Dis. Child.* **51**:868-896 (April) 1936.

1936, cited a case of their own and collected and analyzed the data in 81 additional cases, and Nussey and Miller<sup>1</sup> presented an excellent review of 145 cases in 1939.

#### GENERAL CONSIDERATIONS

*Etiologic Factors.*—The symptom complex is undoubtedly congenital. While heredity is an important factor in the occurrence of other angiomatic conditions, it has been difficult to demonstrate any familial linkage in this particular entity. Cases have been reported from all over the world, the majority coming from Europe. This high European incidence may represent a true geographic relation, or it may indicate that the condition is recognized to a greater extent in Europe.

*Pathologic Features.*—The pathologic process consists in a facial nevus and angiomatic changes in the brain, usually in the form of vascularity of the pia mater overlying the atrophied portion of the brain, with the tissue beneath the angioma infiltrated with calcium. Haines and Pumphrey<sup>7</sup> stated that the brain in their case showed increased resistance to section and the cortex presented a sandy feel. Microscopic examination revealed a decrease in the white matter, which contained small calcified vessels. There was a decrease in the cells of the second and third layers of the cortex, the ganglion cells being atrophied near the calcified areas and glial proliferation conspicuous. Large protoplasmic astrocytes were seen in all layers of the brain. Granular fat cells, indicative of degeneration, were observed in the cortex and the white matter.

The deposits of calcium are of two types: The first type has an "angleworm" configuration, with the gyri outlined in the affected area. Krabbe<sup>8</sup> ascribed this appearance to the calcification of the outer layers of the cortex. These deposits are made up of microscopic granules of lime salts located in the second and third layers of the cortex. The second type presents isolated, relatively homogeneous areas of deposition of calcium with no apparent form or pattern.

*Pathogenesis.*—The pathogenesis of the neurocutaneous vascular abnormalities was described by Luschka<sup>9</sup> who suggested that they arise from sequestration of bits of the embryonic capillary system. Peters<sup>10</sup> expressed the belief that the condition is probably due to atrophy, since neurologic

7. Haines, J. W., and Pumphrey, G. H.: Sturge-Weber Syndrome, *Am. J. Dis. Child.* **61**:557-564, 1941.

8. Krabbe, K. H.: Facial and Meningeal Angiomatosis Associated with Calcifications of the Brain Cortex, *Arch. Neurol. & Psychiat.* **32**:737-755 (Oct.) 1934.

9. Luschka, H.: Cavernöse Blutgeschwulst des Gehirnes, *Virchows Arch f. path. Anat.* **6**:458-470, 1854.

10. Peters, G.: Zur Pathogenese der Sturge-Weberschen Krankheit, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **164**:365-379, 1939.

symptoms rarely appear before the age of 2 years and since microscopic studies at all ages show that all six layers of the cerebral cortex are present. The vascular abnormalities of the brain may be detected by the calcifications and by air studies. The occipital lobe is the most frequently affected site.

*Symptoms.*—Cohen and Kay<sup>11</sup> reported four major symptoms, at least two of which were present in every case of their series. These were convulsions, paralysis, mental retardation and visual disturbances. The visual changes included homonymous hemianopsia, optic nerve atrophy, choked disk, nystagmus, ocular palsies, inequality of the pupils, choroidal atrophy, papillitis, congenital glaucoma (which supposedly is due to venous stasis) and engorgement of the retinal vessels. Some of the more infrequent symptoms were headache, obesity, deafness, tremors, vertigo and impairment of speech. The degree of mental retardation ranged from a faulty memory to temper tantrums, errors in judgment, poor power of concentration and even idiocy.

*Prognosis.*—The prognosis for the unfortunate patients with this disease should be considered from the standpoints of life expectancy and of social and economic adjustment. Actually, their life expectancy is fairly good, even though they are in constant danger from a fatal intracranial hemorrhage. Their economic and mental status is not sound, however, in that they are often of low intelligence and are not capable of earning sufficient money to support themselves, thereby requiring financial aid from their family or the state. They often present a great social problem, the more severely affected persons eventually becoming incarcerated in institutions for the mentally unfit.

*Treatment.*—The efficacy of present day treatment leaves a great deal to be desired. Palliative measures are in the main all that can be offered. Vincent and Heuyer<sup>12</sup> recorded favorable results with radium therapy, and Dyke<sup>13</sup> had some measure of success with roentgen irradiation. Cushing and Bailey<sup>14</sup> expressed the belief that it is foolhardy even to attempt to attack the cerebral angiomas surgically; on the other hand, Dandy<sup>15</sup> asserted that they should be extirpated whenever possible.

11. Cohen, H. J., and Kay, M. N.: Associated Facial Hemangioma and Intracranial Lesion (Weber-Dimitri Disease), *Am. J. Dis. Child.* **62**:606-612 (Sept.) 1941.

12. Vincent, C. L., and Heuyer, G.: Présentation de deux cas d'angiome veineux cérébral, *Rev. neurol.* **1**:509-513, 1929.

13. Dyke, C. G.: The Roentgen Ray Treatment of Tumors of the Brain and Skull, *Bull. New York Acad. Med.* **11**:392-402, 1935.

14. Cushing, H. and Bailey, P.: *Tumors Arising from the Blood Vessels of the Brain*, Springfield, Ill., Charles C Thomas, Publisher, 1928.

15. Dandy, W. E.: Venous Abnormalities and Angiomas of the Brain, *Arch. Surg.* **17**:715-793 (Nov.) 1928.

Pilcher<sup>16</sup> recently reported 3 cases of angiomatous malformations of the brain, 1 of which presented a picture similar to that found in cases of the Sturge-Weber syndrome. The patient responded well to surgical removal of an angioma in the occipital lobe by means of occipital lobectomy. The author, however, described fully the often terrifying hemorrhages from large vessels accompanying such a surgical procedure. Rogers<sup>17</sup> ligated the internal carotid artery and was thus able to give his patient a measurable degree of relief. Sachs<sup>18</sup> described a case in which he applied the procedure of slowly stroking the large vessels with an electrode carrying a weak coagulating current, thereby bringing about a definite recession of symptoms. In addition to these procedures, decompression, together with freeing of adhesions, has also been tried. The mode of treatment to be employed in any case should, of course, be determined by the extent of the lesion, and definite indications for the particular therapeutic measure should exist. On the whole, we believe that the more conservative measures are the methods of choice.

#### REPORT OF CASE

R. F., a white boy, was first admitted to the Mercy Free Dispensary on May 3, 1938, at the age of 13 years. He was the first of three children and was delivered with forceps after his mother had been in labor for twenty-four hours. He was apparently normal, except for the cutaneous manifestation, until he was 7 months of age, when the first convulsion occurred, with twitching of the body and frothing at the mouth. Since that time convulsive seizures had prevailed, with varying frequency. At the time that he first came to the clinic they were occurring about once a month. There was a tendency for the fits to come in bouts of several attacks in one day. At times two or three months passed without his having an attack. The seizures were usually confined to the right side of the body and were characteristically jacksonian. Occasionally they progressed to generalized grand mal seizures with loss of consciousness. At the onset of the convulsion there was an aura, which the boy described as a sensation of his leg "going away." Weakness and incoordination of the right arm and leg had been noticed since the age of 4 years. The child used the left hand predominantly, although none of his ancestors was known to have been left handed. Vision had been poor in his left eye all his life, and a diagnosis of glaucoma of the left eye had been made and an operation advised at another hospital during early childhood. He did poorly in school and had finished only the first grade.

*Examination.*—The patient was rather thin. The head and the upper part of the body were asymmetric, the left side being larger than the right. The asymmetry was especially pronounced in the face, the enlargement of the left maxilla being particularly noticeable. There was an extensive nevus flammeus of the left side of the face, neck and upper part of the chest and the left upper extremity.

16. Pilcher, C.: Angiomatous Malformations of the Brain, *Ann. Surg.* **123**:766-784, 1946.

17. Rogers, L.: Associated Facial and Intracranial Hemangiomas, *Brit. J. Surg.* **21**:229-234, 1933.

18. Sachs, E.: Various Uses of Electrosurgery in the Treatment of Brain Tumors, *South. M. J.* **25**:1013-1019, 1932.

There were moderate weakness and incoordination of the right arm and leg. The tendon reflexes were increased on the right; in addition, the Hoffmann and Babinski responses were elicited on that side. Examination of the perimetric fields showed partial right hemianopsia (fig. 1). Roentgenograms of the skull revealed

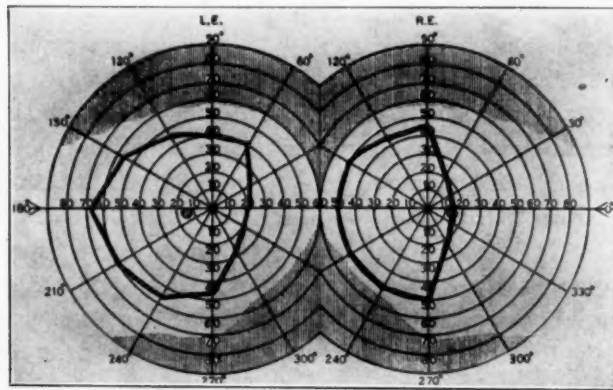


Fig. 1.—Visual fields, showing right homonymous hemianopsia.



Fig. 2.—Photograph of patient, at age of 20, showing extensive port-wine nevus involving the left side of the face, neck and chest and the left upper extremity.

an extensive "angleworm" area of calcification in the left occipital lobe and in the left side of the posterior fossa. There were glaucoma and buphthalmos of the left eye

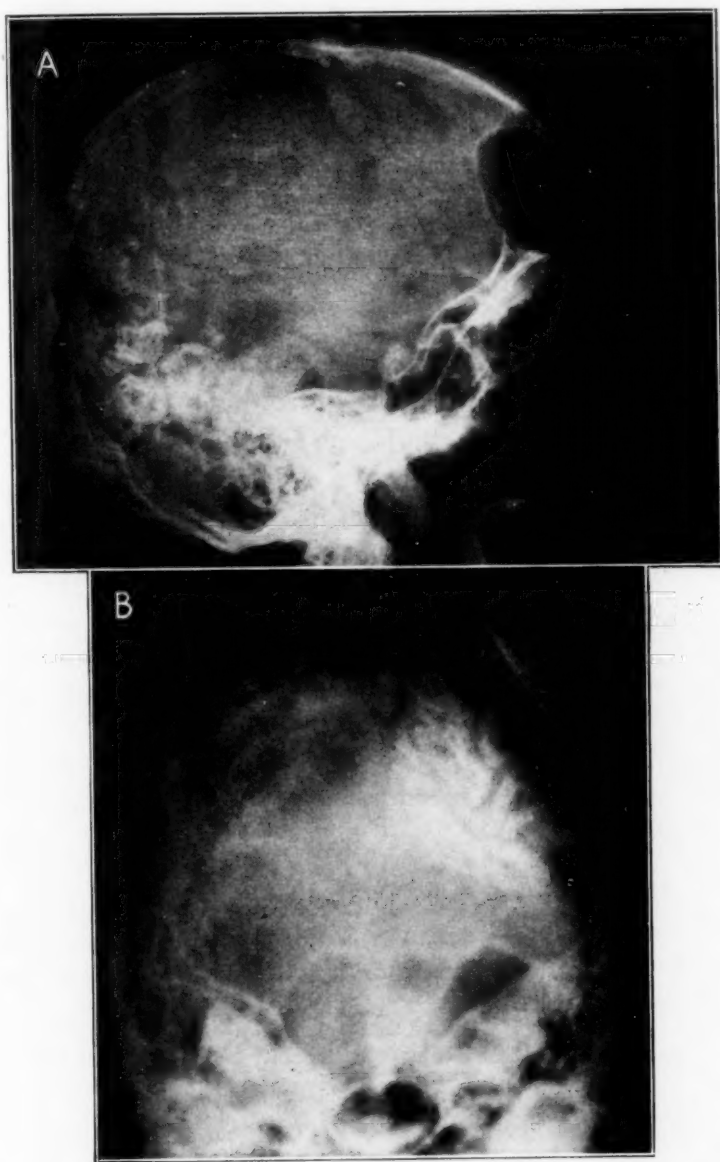


FIG. 3.—Roentgenograms taken at the age of 20. *A*, lateral view, showing the calcification essentially unchanged as compared with earlier films; *B*, roentgenogram showing the "angleworm" configuration.

*Subsequent course.*—In a follow-up visit in November 1945, when the patient was 20, it was learned that he had never gone to school and had been in state institution for mental disease for a six month period on two different occasions, at

his own request, in order to learn a useful craft. However, he seemed never to progress appreciably and was willing to return home at the end of the period. He was still subject to epileptic seizures at monthly intervals, never having been benefited by anticonvulsant drugs. At this time he also confided that he had euphoric dreams.

*Present Status.*—Examination showed that he was fairly well nourished. A port-wine nevus was present on the left side of the face, even extending into the mouth (fig. 2), and involved the left upper extremity and the upper portion of the chest. In addition, there were glaucoma and buphthalmos of the left eye. There was a right hemiparesis; Babinski and Hoffmann responses were elicited on the right side, and the right knee jerk was more active than the left. Furthermore, there was atrophy of the left upper extremity. He was slightly ataxic but the Romberg response was negative. Roentgenograms showed dense deposits of calcium over the left posterior parietal and occipital lobes and in the left cerebellar hemisphere (fig. 3). These deposits tended to outline the convolutions. The posterior clinoid processes seemed to be sharply deflected anteriorly. Comparison of roentgenograms with those taken in 1938 revealed no significant changes.

#### SUMMARY

1. The syndrome of associated facial nevi, intracranial lesions and ocular changes is discussed with regard to the history of its recognition, etiology, pathology, symptomatology and treatment.

2. A case is reported in which the patient has been observed over a period of seven years.

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## FOLLOW-UP STUDY OF MEN WITH PENETRATING INJURY TO THE BRAIN

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THE PURPOSE of this study is to examine the status of men with penetrating injuries to the brain who have been discharged more than six months from an Army neurologic-neurosurgical center. In a previous communication, I<sup>1</sup> described the condition and problems of these men during the later period of their recovery in the hospital. It was acknowledged then that these men had only faint awareness of their problems.

In the present paper is reported the course of their continued recovery outside the hospital and the Army. What problems, defects and symptoms do they have, one or two years after they were wounded; and how are they managing these handicaps? Has the passage of time verified our optimism of what the human organism can endure?<sup>2</sup>

Some, although not all, of these men will require occasional or frequent medical investigation and treatment for many years. It is well, therefore, to know these patients as part of a large group of men similarly injured. What has happened to the others who did not require further medical care? What are the average or common expectations of the group with respect to continued symptoms and disability? In what manner do some deviate from the usual pattern?

### MATERIAL AND METHOD

*Material.*—In a series of 320 men with craniocerebral injury representing consecutive admissions to an Army neurologic-neurosurgical center in the Zone of the Interior during World War II were 100 with surgically proved dural penetration and injury to the brain due to shell fragments or gunshot. Most of these men arrived at the neurologic-neurosurgical center within six months after injury and were hospitalized from three to nine months. A detailed account of their status at that time has been reported previously.<sup>1</sup>

*Method.*—Red Cross social service workers interviewed the same 100 patients, who now had been discharged from the hospital more than six months. In every

1. Aita, J. A.; Late Effects of Injury to the Brain Due to Shell Fragments and Gunshot; Neurologic and Psychiatric Observations, *Arch. Neurol. & Psychiat.* **58**:163-179 (Aug.) 1947.

2. Aita, J. A.: Men with Brain Damage, *Am. J. Psychiat.* **103**:205-213 (Sept.) 1946.

instance this study took place twelve to twenty-eight months after the patient was wounded. Each social service worker based the interview on a detailed questionnaire provided by me.

Almost all patients were found cooperative in this study. A resentful or evasive attitude did not affect our obtaining pertinent data in 4 cases.

#### RESULTS OF INVESTIGATION

*Employment and Education.*—Of the 100 men, 51 were formally employed at the time of interview; 9 others were attending school regularly, 6 of them universities or colleges; 25 had done no work since discharge, and 15 had attempted to work but had quit, for reasons to be explained. The majority of the men who had returned to work or school did so within one to three months after discharge. Of those now occupied, 32 were busy full time (over forty hours a week); 23, for twenty-four to forty hours a week, and 5, for twelve to twenty-four hours a week. Most of these men were doing unskilled, semiskilled and mechanical work. About half were earning \$20 to \$30 per week, and the other half \$30 to \$50 per week. Only 4 had returned to previous jobs.

There was invariably a great deal of indecision and inertia about returning to work or study. There was an ever present fear that veterans' disability pension might be cut or that the site of the wound might be further injured. Many were undecided whether to tell a prospective employer about the injury to the head.

That severity of injury to the brain did not, in itself, explain unemployability was demonstrated by the fact that of 30 men with a diagnosis of severe injury to the brain,<sup>1</sup> 15 were formally employed, although only 2 full time.

*Medical Care.*—At this stage of the follow-up study, 28 men had required further medical attention for symptoms referable to cranio-cerebral injury. Convulsive seizures, headaches, fainting, emotional instability, anxiety, dizziness and fatigue were the chief complaints. Usually the local physician was consulted. Four men with serious personality changes and physical disability required continued hospitalization in a veterans' hospital.

*Veterans' Compensation.*—Disability pension was received by all patients: Five received 25 to 50 per cent compensation; 9, 50 to 75 per cent; 82, 100 per cent and 4, over 100 per cent (additional compensation for visual and hearing loss). All patients receiving less than 100 per cent compensation considered it unsatisfactory at this time.

*Symptoms.*—In the table are listed symptoms persisting one or two years after the injury. Nine men revealed no symptoms or disability whatever. Motor and visual residual symptoms, while very common, were actually less disabling and less bitterly complained of

than were headaches, nervousness and disturbances of consciousness. It is likely that many phenomena tentatively interpreted as fainting, syncope and "black-outs" were actually convulsive in nature.

*Course.*—The course after injury was determined by an objective evaluation of the present status as compared with that at the time of discharge. Sixty-two men presented significant signs of continuing improvement; 30 men showed no improvement, and the condition of 8

*Symptoms Elicited in Follow-Up Study of 100 Men with Penetrating Injuries to the Brain*

	Number of Men
No symptoms or disability.....	9
Residual signs of paresis or paralysis.....	48
Headaches.....	42
(major complaint).....	12
Visual loss.....	33
Pronounced emotional instability; anxiety symptoms.....	25
(severe mood disturbance, such as depression or irritability).....	11
Dizziness.....	22
Striking personality change.....	18
Convulsions.....	15
Incapacitating fatigability.....	14
Excessive sleep.....	12
Hearing loss.....	9
Residual "aphasic" disturbances.....	8
Tinnitus.....	7
Fainting; syncope.....	6
Excessive dreaming.....	6
Diplopia.....	6
Insomnia.....	4

men was considered worse, the progression being illustrated by the following cases:

**CASE 1.**—Unimproved hemiplegia and appearance of frequent convulsions. The patient lives with his father on a farm, works little and walks without a cane. His arm is useless and he now has "black-outs" (several convulsions a month). The physician told his family that nothing could be done for the patient. He continues to have poor vision (homonymous hemianopsia).

**CASE 2.**—Recurrent severe headaches and marital difficulty. The patient has multiple complaints; work of any type causes him to have "black-out spells" (without loss of consciousness), headaches and loss of weight. These symptoms are in contrast to the good impression he made during hospitalization. A distressing marital rift ended in divorce after his return to civilian life. He is satisfied with 100 per cent veterans' disability compensation and sees no need to return to work.

**CASE 3.**—Convulsive seizures, severe depression, alcoholism and attempt at suicide with self inflicted, superficial lacerations of the wrists. Several months after discharge from the hospital, the patient was admitted to a psychiatric clinic. He was severely depressed and uncooperative and refused to eat. The diagnosis was reactive depression. He was unemployed and drank excessively at times. Although he improved considerably after psychiatric care, he continued to complain of frequent headaches, weakness, lack of interest, irritability, bad temper and poor memory. Convulsions, occasional during the first year after discharge, decreased after medication.

**CASE 4.**—Intellectual loss, restlessness and irresponsibility. The patient has not worked since discharge. Because of loss of eyesight, he receives over 100 per cent disability compensation. He bought a car and has been living a nomadic existence, fishing, gambling and mingling with bad company. He gets along badly with his

family, and they are unable to manage him: "He is totally unable to handle his money, has terrific fits of temper and several times has broken furniture." At times the patient himself feels that he can no longer live a "normal life." He continues to complain of headaches, dizziness, poor sleep and "considerable nervousness." Because of excessive appetite he has put on much weight.

**CASE 5.**—Apathy; poor socialization; multiple complaints. The patient is not working, has no hobbies or interests and "does nothing with his time but sit around," complaining of pains in the head and other parts of the body. His family states that this condition represents a marked change in personality. The patient's attitude is apathetic, while that of his family toward him vacillates inconsistently. He has lost a great deal of weight since his discharge.

**Headache.**—Of 61 men who had no headaches during hospitalization, 15 complained of this symptom in the follow-up study; of 39 men who had headaches during hospitalization, 27 continued to complain of headaches in the follow-up study. Throughout the entire study, in the hospital or later, headaches were commonly associated with symptoms of anxiety, emotional instability and dizziness. The continued complaint of headache was commoner among the men with indications of less severe damage to the brain.

**Convulsive Seizures.**—There was a definite description of convulsive seizures in 15 men after discharge, 9 of whom did not have convulsive seizures before discharge. Four men had had a single seizure; the others, three or more. Thirteen of the 15 men had had abnormal electroencephalographic tracings, those of 5 demonstrating focal disturbance.

Nineteen of the 100 men had had seizures at some time during hospitalization but none since discharge; 6 had seizures during hospitalization as well as later. Inclusion of 9 more men in whom seizures developed after discharge from the hospital brings the total to 34 patients who had had at least one convulsive seizure at some time since injury.

For 22 men the onset of convulsions occurred between the fourth and the ninth month after the wound. Of 5 men who had seizures within a month of the wound, none had recurrences. Of 12 who continued to receive anticonvulsant therapy (phenobarbital and/or diphenylhydantoin) after discharge, 6 had at least one seizure despite treatment.

A description of fainting spells appeared in the follow-up study of 6 men, 5 of whom had had no type of seizure while in the hospital. Only 2 had fainted more than twice. All had only borderline abnormal (nonfocal) electroencephalographic tracings while hospitalized.

In the follow-up records of 8 men were descriptions of "black-out spells" associated with dizziness. One of these patients was known to have had previous syncopal attacks, and one other had had a seizure

while in the hospital; 2 had abnormal electroencephalographic tracings with no focal disturbance.

*History of Symptoms of Anxiety and Emotional Instability Elicited in Follow-Up Study.*—Direct, uncoached quotations from social service reports in representative cases follow:

1. "Difficulty meeting people, unable to concentrate, appreciable loss of self-confidence. Afraid to try anything, easily irritable and nervous after visiting people. Three year old son received the brunt of his temper. Dreads leaving his wife to go to the hospital for examination."

2. "Nervous mannerisms, continually passing his hand over the site of his scar. Tense, panic-stricken facies; nervous lump in pit of stomach."

3. "Unable to work because he is too nervous and too weak. Believes that rest and quiet are the only things that will cure him. Has a high temper at times but tries to control it. Is nervous and shaky inside."

4. "'My worst trouble is nervousness. Very often it causes me to vomit, and I have been unable to prevent this. I started on my old job three months after discharge, but I could work only twenty-three days. It was light work, but nervousness pulled me down until I was forced to quit entirely.'"

5. "Social adjustment poor. People in general make him nervous and irritable. He becomes easily upset. Anything that disturbs the even routine of his days bothers him. Since returning from the service, he has no desire to dance or to play cards, which he enjoyed so much previously. Was dismissed from one job because of loss of temper, blamed to nervousness. Poor appetite, spells of irritability and melancholia."

*History of Marked Personality Changes Elicited in Follow-Up Study.*—The following summaries of personality changes in 8 cases illustrate typical problems encountered:

1. "Reactive depression with alcoholism; suicidal attempt."

2. "Irresponsible nomadism; gambling; some intellectual loss."

3. "Previously a dull person, now extremely apathetic, listless and asocial."

4. "Previously happy-go-lucky, irresponsible personality, whose liabilities are now caricatured; alcoholism."

5. "Previously a schizoid, highly intelligent person; continues to be unemployed, devoting most of his time to research. Has a library of books on physics, chemistry and mathematics. Enjoys reading these more than fiction. The patient showed the social service worker copies of many scientific journals, which he reads avidly, frequently writing to the editors when in disagreement with the articles. He continues to be very asocial."

6. "Severe intellectual defect in a patient with previous average intelligence. Memory exceedingly poor. Much nervousness. Cannot stand noise or excitement. Has acquired a bad temper, whereas he used to be good natured. Cannot stand crowds. Unsociable, reserved and shy."

7. "Childlike irresponsibility. Previously superior intelligence. Unemployed for over a year. Hedonistic existence. Believes he deserves a vacation and can see no reason that he should work. Does not mix well with people and attends movies and ball games alone. Does a great deal of fishing. Lacks insight, refuses vocational counseling because he is afraid the counselor will recommend a job in which he is not interested. Is secretive and spends all his veterans' compensation money freely."

8. "Moderate intellectual loss and diminished sociability. All mental processes slowed; much inertia, sleeps a great deal. Experiences periods of "highly nervous state." Poor memory, is negligent and forgets where he puts things. Is content to remain alone and live a drab existence. Has completely lost confidence in himself and feels extremely inferior to others. Is always afraid he will not be able to do things as well as the next person or that he may injure himself."

#### DEATHS

The follow-up study disclosed only one death. This occurred accidentally in the crash of a motor cycle which the patient was driving. Whether or not he suffered loss of consciousness or a seizure is not known. He had had no such episode previously, and his electroencephalogram had been normal.

#### INTRAGROUP ANALYSIS

The extent of continued disability in this group of unselected survivors varied directly with the clinical estimation of severity of damage to the brain. Patients with less severe injury retained more intact assets regardless of frequent subjective distress. Those fortunate enough to have had previous good integration and resources, careful convalescent management, healthy home environment and continued efforts at rehabilitation did well. In the cases of less severe injury to the brain, these factors became of greater significance in determining the extent of disability.

#### SUMMARY

One hundred men with penetrating damage to the brain were followed for more than six months after discharge from an Army hospital (one to two years after injury). Sixty were found formally employed or attending school.

Twenty-eight had required further medical care for symptoms referable to craniocerebral injury. Only 4 were institutionalized for continued care in veterans' hospitals.

Paralysis, hemianopsia, sensory loss and even residual "aphasic" signs were of less concern to the patient than were disturbances of consciousness, headache and emotional reactions.

Sixty-two men showed significant and continued improvement. Headaches were commoner among those who had them while hospitalized and those with less severe damage to the brain.

At the time of follow-up study, 34 men had had at least one convulsive seizure. The onset of such seizures was usually between the fourth and the ninth month after the wound was received.

Extent of disability is determined by the severity and location of intracranial damage and by the multiple social and personality factors borne by the patient who experienced the injury.

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## SLEEP-ELECTROSHOCK THERAPY OF THE PSYCHOSES

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**S**LEEP-ELECTROSHOCK therapy is a modification of electroshock therapy which utilizes the preliminary induction of sleep prior to the passage of the electric current.<sup>1</sup>

Since Sakel's original observations in 1928 of hypoglycemic (shock) treatment of the psychoses,<sup>2</sup> a method encumbered by its demands on personnel and time, it had been hoped that a simpler procedure would be forthcoming. The introduction of "metrazol" therapy by von Meduna<sup>3</sup> in 1934, with its simple intravenous injection, was, therefore, enthusiastically received. The fear induced in most patients so treated, however, soon revealed the failing in this procedure. Therefore, when, in 1938, Cerletti and Bini<sup>4</sup> published their method in which the patient remained completely amnesic for events from the moment coincident with the passage of the electric current, it appeared as if the ideal in shock therapy had been attained.

However, in actual experience it soon became apparent that orthodox electroshock was inapplicable to a number of patients who might otherwise have been expected to profit from such treatment. Such patients include those who have acquired a fear of the treatment and those who react to electroshock with marked psychomotor irritability.

It is the purpose of this communication to describe the method whereby both these difficulties were successfully circumvented.

Briefly stated, the method consists in the intravenous injection of 2.5 to 5 per cent "pentothal-sodium" administered through a period of approximately one minute, by which time the patient is asleep. Usually, 4 to 8 cc. of the 5 per cent solution is required. The 2.5

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From the Alfred Ullman Laboratory, Sinai Hospital.

1. Rubinstein, H. S.: Sleep-Electro-Shock Therapy, *Science* **101**:430; 1945.
2. Sakel, M.: The Nature and Origin of Hypoglycemic Treatment of Psychoses, *Am. J. Psychiat.* **94**:24, 1948.
3. von Meduna, L.: General Discussion of the Cardiazol Therapy, *Am. J. Psychiat.* **94**:40, 1938.
4. Cerletti, U., and Bini, L.: L'elettroshock, *Policlinico (sez. prat.)* **45**:1261, 1938.

per cent solution is best administered at the very slow rate of approximately 1 cc. per minute, when the patient may be kept on the verge of actual sleep for varying intervals, during which time he may be questioned in accordance with narcoanalytic principles<sup>5</sup> in an attempt to elicit psychogenic material.

Regardless of the rapidity of induction, the depth of the patient's narcosis may be rather simply gaged. In very deep sleep the corneal reflex is absent. With the progressive approach toward consciousness, the corneal reflex returns first; then, the cutaneous reflexes become elicitable, and finally, just prior to awakening, the motor mechanism is released.

While the patient is still asleep, the minimal convulsant dose of electricity is administered through frontal electrodes in the usual way. The dose may vary from 70 to 130 volts applied for two-tenths to one-tenth second with different patients. As in the orthodox method, the effective dose, when once determined for a patient, must be slightly increased from time to time as treatments are repeated.

The intensity of the reaction can usually be controlled by carefully choosing the depth of anesthesia at which the electric current is closed. For example, when the patient is deeply asleep, as judged by the intact corneal reflex with absence of the cutaneous response, a minor reaction usually results. This is characterized by a single clonic jerk. With the release of cutaneous reflexes, conveniently tested by stroking the lower eyelid with a wisp of cotton, the closing of the circuit results in a reaction of medium intensity, as manifested by a convulsion, usually limited to the face or the face and shoulders. If the current is applied at a still higher level of consciousness, when the motor mechanism is released, a major reaction, characterized by a generalized convulsion indistinguishable from that observed in orthodox electroshock, is obtained.

It will be recalled that sleep-electroshock therapy is indicated when a patient who has already received treatment has reacted with strong psychomotor agitation, or when a patient, either before or after orthodox electroshock, discloses an intense fear of shock therapy.

The following case reports are illustrative:

#### REPORT OF CASES

CASE 1.—D. L., a white man, married, aged 34, was seen in a state of reactive depression. A grocery clerk by occupation, he was the sole support of his wife and three small children. He had always been a rather serious person, who had worked zealously for a chain store company with the hope that a promotion would augment his rather meager income. Finally, while still fatigued from overwork and long hours, he was placed in charge of a new and large store. There his elation was

5. Horsley, J. S.: *Narco-Analysis*, London, Oxford University Press, 1943.

short lived, for he found the new situation entirely too demanding. Work piled up, so that he gradually came to feel that he "was slipping." He became terrified over the prospects of failure, became tense and sleepless, and found himself beginning another job before the task at hand had been completed. He became confused, accused his employers of purposely placing him in the new situation so that he might fail and thus justify their intention to "dismiss" him. Because he foresaw only hopelessness in his future, he made a suicidal attempt by taking an overdose of "sleeping pills."

On examination, the patient was obviously depressed and weepy and uttered expressions of self depreciation and hopelessness; his concentration was poor, and he had completely lost his interests.

On Aug. 6, 1945, he was given an electroshock treatment, to which he responded with such violent combativeness that for almost half an hour his undirected and unleashed fury knew no bounds—he shouted, kicked, butted and wrestled. It was with the greatest difficulty that a tragic accident was avoided. Twelve sleep-electroshock treatments administered thereafter at a rate of three a week were each followed by a calm which was indeed a relief to all concerned, and the patient, whose treatment could thus be continued, made an excellent symptomatic recovery.

CASE 2.—E. D., a white man, single, aged 28, was first seen in March 1945, when he was found to be mentally defective (high grade moron) in a state of hebephrenic schizophrenia. His learning capacity was limited, so that at 17 years of age he quit school, in the seventh grade, to go to work. After several unsuccessful attempts, he finally got a job in a steel plant and worked successfully at an assigned routine for two and a half years. He then became overly persistent in his attempt to be transferred to another task and was discharged. Shortly thereafter (July 1941) he became tense, found it difficult to sleep and acquired the notion that he was hurting other people's feelings. He became seclusive, then confused, and then disorderly and obnoxiously aggressive. A month later he was admitted to a state hospital. He remained here for six months, when, on quieting down, he was paroled (March 1942). He then worked around the house and seemed to get along satisfactorily until August 1944 (more than two years later), when he was observed to kneel as though in prayer and spoke irrelevantly. He was returned to the state hospital, where he was found to be completely confused and hallucinated. He showed no signs of improvement for the next four months, so in January 1945 a course of electroshock therapy was started, with two treatments weekly. By March 1945, after receiving twenty-nine treatments, he became sufficiently calm and cooperative to be sent home, with instructions to continue maintenance electroshock therapy extramurally.

When seen in March 1945, just after leaving the hospital, he was neatly clad and fairly well orientated and friendly, but acted silly and frequently laughed without provocation in a meaningless fashion. As yet, he had made no attempt to carry out any of the household duties which he had assumed prior to his second admission to the hospital.

Between March and July 1945 the patient was given a total of thirty-two electroshock treatments, at a rate of two a week. Gradually he began to assume more and more of his preillness duties and gave up his tendency to silly laughter. As his mental state cleared, however, he acquired fear of treatment, an attitude which was first suspected when he displayed restlessness bordering on agitation on the day scheduled for his treatment. On such days he would sweat profusely, peer in staring fashion and tremble visibly. It was then that sleep-electroshock treatments were instituted. These were given at first twice a week. With progressive improvement, the intervals between treatments were gradually extended, so that

by November 1945 the treatment-free interval had been increased to two weeks. He was then discharged. His behavior since November 1945 has been entirely satisfactory as judged by his preillness personality limitations.

In all, the patient has had a total of seventy-eight treatments. The last seventeen of these were sleep-electroshock treatments, without which he would certainly have had to be returned to the state hospital.

Twenty-five other patients were treated by this method. This total of 27 patients included 9 with acute depressions, with 9 symptomatically cured; 8 with chronic depression, with 3 symptomatically cured, 2 showing improvement and 3 showing no improvement; 1 with involutional melancholia, with symptomatic cure; 1 with mixed psychosis, with symptomatic cure; 5 with schizophrenia, with 1 symptomatically cured, 2 showing improvement and 2 showing no improvement; 1 with depression associated with chronic alcoholism, whose depression cleared but whose alcoholism remained unaffected; 1 with an acute obsessive-ruminative tension state with schizophrenic features, whose symptoms became completely cleared, and 1 with a chronic obsessive-ruminative tension state with depressive features, whose depression was lifted but whose deeply ingrained neurotic pattern persisted.

#### COMMENT

Shock treatment has now attained a useful place among the therapeutic methods directed toward alleviating selected psychiatric disorders. Each of these shock methods has its specific value, but each, likewise, has its limitation. Electroshock therapy has been able to reach the greatest number of patients because of its relative simplicity of administration. A growing fear after several treatments or a pronounced combativeness, already noted after the first treatment, has made electroshock inapplicable to patients who might otherwise have been expected to profit from this form of therapy. Because of such fear, several depressed outpatients had discontinued their treatment and had then rather promptly entered into a maniacal state, for which commitment to an institution had become necessary.

Likewise, danger is associated with an overly excited patient who, because of difficult manageability, becomes a threat to himself, to those in attendance and, especially in office practice, to the surrounding equipment.

Fortunately, both these difficulties were overcome by sleep-electroshock therapy, as here presented. In fearful patients, sleep is induced before the electrodes are applied, so that the patient remains unaware that electricity is used. In such cases, however, a responsible member of the family is consulted and informed of the method before it is applied.

In the case of patients reacting with psychomotor excitability the electrodes may be applied first and the injection of "pentothal" given

afterward. Parenthetically, it has already been noted that some patients who have no fear of the treatment but who react with excitability are terribly afraid of a needle. With such patients the injection of "pentothal" is deferred until immediately after the patient has completed an electrically induced convulsion and has reestablished normal breathing.

It is interesting that when sleep is first induced the degree of response to the electrical stimulus can be controlled in accordance with the depth of anesthesia. It is important in this regard to avoid applying the current if the corneal reflex is absent, since this indicates a depth of anesthesia which is dangerous for this purpose. With only the corneal reflex present, the response to electrical stimulation is minor; with cutaneous reflexes present, the response is of medium intensity, and when the patient begins to move spontaneously, i.e., shows evidence of motor release, the expected major convulsive seizure results.

The ability to apply a convulsant dose of electricity and yet avoid a convulsion in the deeply anesthetized patient raises the question whether such a dose of electricity will, even in the absence of a convulsion, yield the beneficial results which have heretofore been attributed to the convulsion.

From the standpoint of curative influence, it is quite certain that sleep-electroshock therapy has about the same effect on the symptoms of the different types of illness as orthodox electroshock. Briefly stated, it is practically specific for the affective disorders, especially the depressions; it is helpful in some cases of schizophrenia but leaves the psychoneuroses practically unaffected. It must be stressed that "cures" relate to symptoms only, since the patient gains no added insight unless his comforts are resolved through subsequent psychotherapy.

With respect to the concomitant use of sedation and electroshock, it is interesting to note that already in 1943 Wortis<sup>6</sup> used intravenous injection of "sodium amytal" before induction of convulsions in order to allay the anxiety often connected with electroshock treatment. However, it was evidently the purpose in that treatment to avoid actual sleep before applying the current, since the dose of "sodium amytal" was actually diminished with patients who had fallen asleep prior to the application of current. While such a procedure will undoubtedly diminish the psychomotor excitability in patients so disposed, it has no application to patients who fear the orthodox procedure or the manipulations—such as the applications of electrodes—related thereto.

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6. Wortis, S. B.: Modifications of Electrofit: Sodium Amytal, *Am. J. Psychiat.* **100**:358, 1943.

The real importance of sleep-electroshock therapy is that it not only permits the continuation of "maintenance shock" therapy<sup>7</sup> of many patients who, as they advance toward health, refuse to cooperate but, through its sedative effect, spares the more excitable patients the tremendous strain which such overactivity adds to that of the convulsion itself. For this reason, it has found usefulness in the treatment of the aged. In addition, the restraining effect of "sodium pentothal" on the convulsion has even permitted the continuation of treatment in a patient who had previously sustained a crushing injury of one of the thoracic vertebrae.

Finally, one must consider the danger of the simultaneous use of a barbiturate and electricity, either of which when administered in lethal quantities affects primarily the respiratory centers in the medulla. For this reason, it is important that corneal reflexes be intact before the electric current is applied.

#### SUMMARY

Sleep-electroshock therapy is a modification of the orthodox electroshock treatment in which the patient is induced to sleep by the intravenous injection of "sodium pentothal" prior to the application of the electric current. By this means patients who would themselves have discontinued shock therapy because of fear and patients who, because of their unmanageable psychomotor reactions, would have to be denied treatment by the physician, have been treated successfully.

No complications have been observed in the course of over five hundred treatments. On the contrary, by the careful gaging of the depth of anesthesia, one may selectively evoke minor, medium or major reactions.

Sinai Hospital (5).

7. Kerman, E. F.: Therapeutic Efficacy of Electroconvulsive Therapy, *J. Nerv. & Ment. Dis.* **102**:221, 1945.

The Abbott Laboratories supplied the "pentothal sodium" for this investigation.

## Case Reports

### EROSION OF THE ANTERIOR CLINOID PROCESSES SIMULATING THAT DUE TO INTRASellar TUMOR

#### A Diagnostic Pitfall

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THERE HAS always been some mystery connected with the changes in the anterior clinoid processes caused by intracranial tumors. It is frequently difficult to distinguish roentgenographically the sellar changes due to an intrasellar tumor from those due to a suprasellar tumor or to generalized increase in intracranial pressure. The anterior clinoid processes are really lateral to the pituitary body and may not be eroded by early enlargement of this gland.<sup>1</sup> However, Twining<sup>2</sup> suggested that such growths press the internal carotid arteries against these bony structures, which are worn away by the water hammer of the pulse, and not by the direct pressure of the tumor itself.

Roentgenographic study of a recent case revealed enlargement of the sella turcica and hollowing of the under surface of each anterior clinoid process. These observations seemed to indicate that there was an enlarging mass within the sella. Otherwise, how could the inferior surface of each anterior clinoid process be eroded? In fact, there was a tumor, but it lay not within the sella but in the posterior fossa. A report of this case, with an explanation of the paradoxical roentgenologic findings, is the basis of this paper.

#### REPORT OF CASE

*History.*—A white man aged 46, a dairy farmer, was admitted to the hospital on Nov. 20, 1946, having been referred by Dr. Jerome Alderman. He complained chiefly of headaches, but had also noted impairment of memory, change in personality, blurred vision and intolerance of odors. Twelve years before admission, for a year or two, the patient had had severe headaches when he bent over to play with his children. Morning headaches, referred to the vertex of the skull, be-

1. Schüller, A.: The Sella Turcica, *Am. J. Roentgenol.* **16**:336-340 (Oct.) 1926.

2. Twining, E. W., cited by Jefferson, G.: Extrasellar Extensions of Pituitary Adenomas, *Proc. Roy. Soc. Med.* **33**:440 (May) 1940.

gan in March 1945. They became severe in August 1945 and were associated with vomiting in December 1945. Turning of the head or change of posture began to aggravate the headaches, which recurred intermittently. In August 1946 he noticed that the odors of cooking or of the barn nauseated him and that he had become increasingly irritable. Thereafter, he exhibited poor memory for both recent and remote events. In the same period, he also began to have blurring of vision and staggering gait. The family and the past history were noncontributory.

*Examination.*—The patient was well developed and well nourished and appeared alert and cooperative, but his memory was poor. General examination revealed nothing abnormal. Neurologic examination revealed mild bilateral deafness of the nerve type, but nothing else of significance except for the changes referable to the eyes. The right optic disk was chronically choked and elevated 2 to 3 D. The left optic disk was pale temporally, but there was edema nasally of approximately 1/2 D. Visual acuity was 20/20 in the right eye and was limited to light perception at 8 feet (240 cm.) in the left eye. Examination of the fields of vision



Fig. 1.—Lateral view of the sella turcica.

revealed concentric contraction in both eyes, but neither scotoma nor disturbance of color perception. The ophthalmologist expressed the belief that the left optic nerve had undergone primary atrophy, on which papilledema had been superimposed. He suggested the possibility of a Foster Kennedy syndrome due to a tumor at the base of the left frontal lobe.

Electroencephalographic examination revealed major changes over both frontal lobes, which were more pronounced on the right than on the left. Potentials of 1 1/2 to 3 cycles per second, with an amplitude of about 200 microvolts, were demonstrable synchronously over the right and left frontal areas. The electroencephalographic impression was that of a rapidly growing lesion, probably near the midline in the frontal region. Roentgenographic examination of the skull revealed enlargement of the sella, erosion of the structure of the posterior clinoid processes and

dorsum sellae and erosion of the under surface of each anterior clinoid process (fig. 1). The roentgenologic impression was that of intrasellar tumor.

At this point, it was considered that the patient had an intrasellar tumor which had extended forward to involve the left optic nerve and upward to encroach on and block the third ventricle. Angiograms of the right side of the brain, made after the percutaneous injection of 12 cc. of 35 per cent iodopyracet injection U. S. P. into the common carotid artery, revealed that the middle cerebral artery had been displaced upward throughout its course. This observation was consistent with internal hydrocephalus. However, because of a lingering doubt concerning the diagnosis, ventriculograms were made and revealed dilatation of both lateral ventricles and of the third ventricle. Furthermore, they showed an angulation of the aqueduct which was characteristic of a tumor of the posterior fossa (fig. 2).

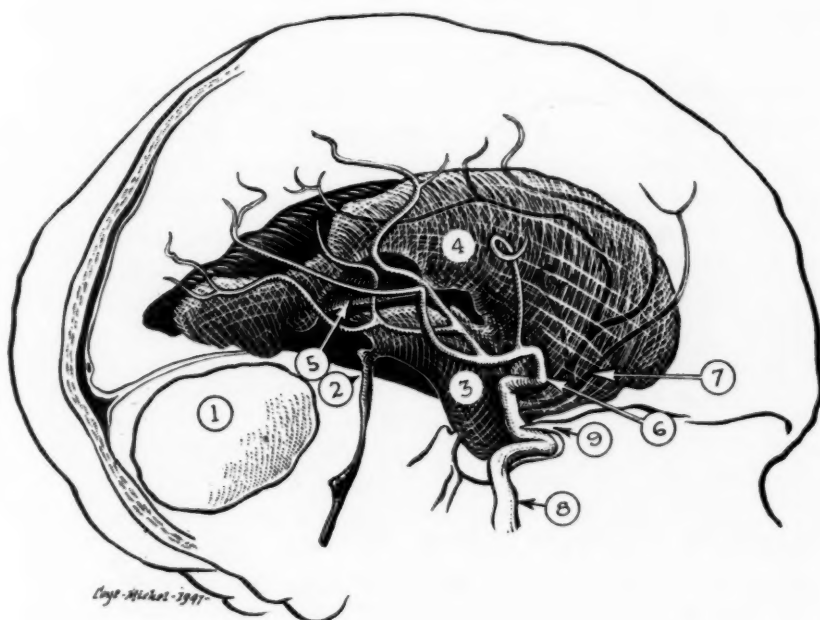


Fig. 2.—Composite drawing based on tracings from the angiograms and ventriculograms in this case. The structures designated by the numerals are explained in the text.

*Operation.*—On Nov. 27, 1946, exploration was made through a midline cervico-occipital incision, revealing an intradural tumor in the place normally occupied by the superior portion of the vermis. The tumor measured 5 by 6 by 5 cm., was lobulated, very firm and vascular and may have been attached to the inferior surface of the tentorium. The center of the tumor was slightly to the left of the midline. As far as could be determined, the growth was removed completely.

*Subsequent Course.*—Convalescence was stormy and was marked by an accumulation of cerebrospinal fluid among the muscles of the neck. This complication responded promptly to a second operation, with obliteration of the tiny dural defect through which spinal fluid had gained access to the superficial layers of the wound.

On discharge from the hospital, on Jan. 31, 1947, the patient's wound was well healed and his neck was not stiff. There were moderate signs of cerebellar involvement in both lower limbs and in the right upper limb. Visual acuity was greatly impaired in the left eye and slightly impaired in the right eye. The subsequent course was one of steady improvement.

#### COMMENT

In this case of tumor of the posterior fossa, the erroneous diagnosis of primary intrasellar tumor with suprasellar extension was originally made through roentgenographic and clinical studies and was apparently confirmed by electroencephalographic and ophthalmologic data. Routine ventriculograms failed to correct this erroneous impression, but, by good fortune, additional views were requested. These revealed kinking of the aqueduct in the fashion characteristic of tumor of the vermis.

It is now known that electroencephalographic disturbances in the frontal lobe may arise from a pathologic lesion in the contralateral lobe of the cerebellum, presumably as a result of disturbance of the cerebellopontofrontal tract.<sup>3</sup> Hence, the bifrontal disturbance, which was greater on the right side than on the left, is explained on the basis of a midline cerebellar lesion which extended more to the left than to the right. Simulation of the Foster-Kennedy syndrome by a cerebellar tumor has been previously reported.<sup>4</sup> There remain for further elucidation, the sellar changes which were demonstrated in the roentgenograms.

The roentgenographic diagnosis of an intrasellar tumor may be made unequivocally in the early stages of sellar erosion. There may be increases in the anteroposterior diameter and in the depth of the sella, both of which may be associated with hollowing of the anterior surface of the dorsum sellae. There may be asymmetric erosion of the floor of the sella or partial destruction of one anterior clinoid process. However, once the dorsum sellae has completely disappeared, it may not always be possible to distinguish the effects of intrasellar growth from those of ventricular distention or from tumors outside the sella turcica.<sup>5</sup> Thus, bilateral symmetric distortions of the anterior clinoid process are of no value in making such a differentiation.<sup>6</sup> The

3. Jasper, H. H.: Personal communication to the author.

4. Wagener, H. P., and Cusick, P. L.: Chiasmal Syndromes Produced by Lesions in the Posterior Fossa, *Arch. Opth.* **18**:887-891 (Dec.) 1937.

5. Pancoast, H. K.; Pendergrass, E. P., and Schaeffer, J. P.: *The Head and Neck in Roentgen Diagnosis*, Springfield, Ill., Charles C Thomas, Publisher, 1940.

6. Schüller, A., cited by Cairns, H., and Jupe, M. H.: Central Nervous System, in Shanks, S. C.; Kerley, P., and Twining, E. W.: *A Text-Book of X-Ray Diagnosis* London, H. K. Lewis & Co., Ltd., 1939, vol. 3, p. 53.

erosion of both anterior clinoid processes from above is usually due to a suprasellar mass, most commonly a dilated third ventricle.

However, in the present case there was erosion of the under surfaces of the anterior clinoid processes. A suggested explanation of this phenomenon is illustrated by figure 2, a composite drawing based on direct tracings from the angiograms and ventriculograms in this case. The numbers in the figure indicate the following structures: (1) the tumor itself; (2) the blocked aqueduct, which was kinked between the superior and the inferior colliculi, so well described by Twining;<sup>7</sup> (3) the grossly dilated third ventricle, the anteroinferior end of which has entered and enlarged the sella, displacing backward and eroding the posterior clinoid processes; (4) the right lateral ventricle; (5) the site of attachment to the body of the ventricle of the temporal horn, removed from the drawing to avoid confusion; (6) the middle cerebral artery, displaced upward "en diagonale,"<sup>8</sup> owing to dilatation of the temporal horn of the lateral ventricle; (7) the anterior cerebral artery, the supracallosal portion of which has been elevated owing to dilatation of the anterior horn of the lateral ventricle; (8) the internal carotid artery, and (9) the anterior clinoid process. It is worth recalling that the internal carotid artery, which has been passing along the lateral aspect of the sella, ascends out of the sella on the medial aspect of the anterior clinoid process. It is also significant that in this case the supraclinoid portion of the internal carotid artery ascended practically in a vertical direction.

The probable sequence of events in this case can now be reconstructed. The enlarging tumor caused compression, kinking, blockage of the aqueduct and internal hydrocephalus.<sup>9</sup> Enlargement of the third ventricle resulted in posterior displacement and erosion of the posterior clinoid processes. Ballooning of the lateral ventricle produced elevation of both the anterior and the middle cerebral artery, which, in turn, caused traction on the terminal, supraclinoid, portion of the internal carotid artery. Thus, the pulsating artery came to erode the inferomedial aspect of each anterior clinoid process.

#### SUMMARY

There is presented a case of cerebral tumor in which roentgenographic studies revealed destruction of the posterior clinoid processes,

7. Twining, E. W.: Radiology of the Third and Fourth Ventricles, Brit. J. Radiol. **12**:385-418 (July) 1939.

8. Moniz, E.: L'angiographie cerebrale, Masson & Cie, 1934.

9. Twining, E. W.: Radiology of the Third and Fourth Ventricles, Brit. J. Radiol. **12**:569-600 (Oct.) 1939.

enlargement of the sella turcica and hollowing erosion of the under surface of the anterior clinoid processes. The tumor was not intrasellar but cerebellar. It is suggested that the tumor blocked the aqueduct, thus causing dilatation of the third and the lateral ventricles. This dilatation caused elevation of the anterior and middle cerebral arteries, which exerted upward traction on the terminal portion of the internal carotid artery. The pounding of the latter eroded the inferomedial aspect of each anterior clinoid process.

Physicians Building.

## Case Reports

### EFFECT OF ALBUMIN SOLUTION ON CEREBROSPINAL FLUID PRESSURE

FREDERICK A. FENDER, M.D.  
AND

ALEXANDER S. MacKENZIE, M.D.  
SAN FRANCISCO

**T**WO EXPERIMENTS were carried out on a patient to determine the effect on the cerebrospinal fluid pressure of intravenously administered 25 per cent solution of human albumin.<sup>1</sup> The patient was a man aged 27 with a cerebral tumor. Two attempts to remove the tumor had shown that it was inoperable and rather vascular (sarcomatous meningioma). The patient had been left with a "riding" bone flap.

#### EXPERIMENTAL STUDY

The setup was the same in the two experiments. A manometer and a connecting tube were filled with isotonic solution of sodium chloride. The patient lay on his side with the bone flap uppermost. After a period of rest in bed, lumbar puncture was carried out, and the subarachnoid space was connected with the recording system. Only a few drops of cerebrospinal fluid were lost in this process, and, since the manometric system had been filled, no cerebrospinal fluid escaped into it.

After a period of observation to establish a base line, the albumin solution was injected intravenously. Thereafter, readings of the cerebrospinal fluid pressure were made at fifteen minute intervals.

In the first experiment the infusion was carried out slowly, two hours being required for its completion. In the second, the infusion was carried out rapidly, in a period of ten minutes. Experiments were terminated when it was thought that a sufficient time had elapsed to demonstrate the effect of the injected material. Scrupulous care was taken to record the pressure under exactly "basic" conditions. The patient's upper and lower extremities were adjusted to the same positions during each recording. His head was kept at the same elevation on a firm pile of folded blankets. This "pillow" was not allowed to exert any compression on the juglar vein.

At the termination of the second experiment, it was found that the removal of approximately 10 cc. of fluid lowered the pressure from a level of 450 mm. to one 150 mm. of water. As will be seen, there was diuresis. In the second experiment,

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From the Department of Surgery, Stanford University School of Medicine.

1. Dr. Arthur L. Bloomfield sent us the material, which was furnished by the Cutter Laboratory, of Berkeley, Calif., for investigative use. It was salt free and was preserved with 0.02 molar solution of sodium caprylate.

the blood protein level was measured just before the experiment began and within five minutes after its termination. The level was found to be 7 Gm. per hundred cubic centimeters in each case.

The possibility that a "riding" flap may have affected the pressure measurements is unlikely in view of the following observations: At the end of the second experiment the escape of a few cubic centimeters of cerebrospinal fluid lowered

## EXPERIMENT I—MARCH 7, 1947

Elapsed Time	Pulse Rate	Respiratory Rate	Blood Pressure	Cerebrospinal Fluid Pressure Mm.	Comment
00:00	72	20	118/88	—	
00:30	80	20	124/78	—	
00:50	—	—	—	550	Lumbar puncture (initial pressure)
01:00	80	20	112/70	480	
01:10	76	20	112/68	480	
01:15	—	—	—	—	Intravenous injection of 25% albumin solution started, 12 drops a minute
01:30	—	—	—	480	
01:45	72	20	112/70	440	
02:00	—	—	—	440	Lunch
02:15	72	20	110/68	450	
02:30	—	—	—	460	
02:43	—	—	—	—	Rate of injection of albumin increased to 24 drops a minute
02:45	82	20	110/74	480	
03:00	—	—	—	460	
03:10	—	—	—	—	Patient uncomfortable; voided 20 oz. of urine
03:15	82	18	120/74	440	
03:25	—	—	—	—	Intravenous injection completed
03:30	—	—	—	440	
03:45	76	18	112/72	450	
04:00	—	—	—	450	
04:15	76	18	112/68	450	
04:30	—	—	—	440	
04:45	78	16	114/72	440	
05:00	—	—	—	450	
05:15	76	20	118/70	450	
05:25	—	—	—	—	Cup of coffee
05:30	—	—	—	450	
05:45	78	20	118/78	390	
06:00	—	—	—	450	
06:15	74	18	108/70	440	
06:30	—	—	—	450	
06:35	—	—	—	—	Patient voided 16 oz. of urine
06:45	82	18	122/80	460*	
07:00	—	—	—	450	
07:15	78	18	122/74	440	
07:30	78	18	124/84	440	Readings terminated

## EXPERIMENT II: MARCH 13, 1947

Elapsed Time	Pulse Rate	Respiratory Rate	Blood Pressure	Cerebrospinal Fluid Pressure Mm.	Comment
00:00	—	—	—	—	Voided 20 cc.
00:15	—	—	—	—	In bed, relaxed
00:30	80	24	112/70	—	In bed, relaxed
00:45	82	20	118/78	—	In bed, relaxed
01:00	80	16	112/68	—	In bed, relaxed
01:10	—	—	—	440	Lumbar puncture (initial pressure)
01:15	90	18	108/68	420	Resting, basal state
01:30	88	18	108/70	450	Resting, basal state
01:33	—	—	—	—	Intravenous injection of 25% albumin solution started
01:43	—	—	—	—	Intravenous injection completed
01:45	80	20	106/78	440	
01:50	—	—	—	—	Took 240 cc. of fluid
02:00	80	20	98/68	410	
02:15	80	16	108/78	430	
02:30	88	18	118/84	420	
02:45	84	20	118/84	430	
03:00	84	16	110/78	430	
03:15	86	18	122/78	450	
03:30	84	18	120/80	440	
03:45	78	18	112/78	450	Readings terminated

the pressure to a final level of 150 mm. of water. Subsequently, also, lumbar puncture was carried out repeatedly. In each case the cerebrospinal fluid pressure was materially reduced by the escape of small amounts of cerebrospinal fluid. The protocols follow.

## CONCLUSION

Under the conditions of this experiment, a 25 per cent solution of albumin, given either rapidly or slowly, had no effect on the cerebrospinal fluid pressure.

2209 Webster Street (15).

## News and Comment

### FOURTH INTERNATIONAL NEUROLOGICAL CONGRESS

The Fourth International Neurological Congress will be held in Paris, France, from Monday, Sept. 5 to Saturday, Sept. 10, 1949, inclusive. In accordance with the usual custom, one day, probably Wednesday, will be devoted to excursions in the vicinity of Paris.

The officers of the Fourth Congress are: honorary presidents, Sir Charles Sherrington, Prof. Gordon Holmes, Prof. Georges Guillain, Dr. Andre-Thomas; president, Prof. T. Alajouanine; first vice president, Dr. J. A. Barre; vice presidents representing various constituent countries, as follows: Argentina, Professor Dimitri; Belgium, Professor van Gehuchten; Brazil, Professor Austregesilo; Canada, Professors Penfield and Saucier; Chili, Professor Asenjo; Czechoslovakia, Professor Henner; Denmark, Professor Krabbe; England, Professor Feiling; Greece, Professor Pamboukis; Netherlands, Professor Brouwer; Norway, Professor Monrad-Krohn; Peru, Professor Trelles; Poland, Professor Opalski; Spain and Portugal, Professor Moniz; Sweden, Professor Antoni; Switzerland, Professor de Morsier; Turkey, Professor Uzman; United States, Professor Riley; Uruguay, Professor Schroeder (a vice presidential vacancy is held for each of the following countries, which at last report had not responded: Finland, Union of Soviet Socialist Republics, Yugoslavia); secretary general, Dr. Raymond Garcin, 19 rue de Bourgogne, Paris VII<sup>e</sup>; local secretary, Dr. Jean Sigwald; assistant secretary, Dr. Guilly; treasurer, Mme. Dr. Sorrel-Dejerine.

The French National Committee as now constituted consists of Drs. Guillain, Alajouanine, Andre-Thomas, Baudouin, Clovis Vincent, Lhermitte, Tournay, Barre, Riser, Roger, Delmas-Marsalet, Dechaume, Garcin, Mme. Sorrel-Dejerine, Sigwald and Guilly, with the program chairmen, Drs. Brouwer, Krabbe, Riley and Feiling, *ex officio* members of the committee.

The precise location of the headquarters of the Congress and the places where the sessions will be held will be determined by the French committee, and later notices will provide this information.

The program executive committee, which met in Paris in July 1947, selected four topics for the morning sessions of the Congress. The subject of each symposium and the persons entrusted with the preparation of these special topics are as follows: (1) The Thalamus and Its Pathology, Dr. Bernardus Brouwer; (2) Electroencephalography and Electromyography, Dr. Knud Krabbe; (3) Virus Diseases of the Nervous System, Dr. Henry Alsop Riley; (4) Surgical Treatment of Pain, Dr. Anthony Feiling.

The program for each of these chosen subjects will be prepared by the chairman in charge, and about four invited speakers will be selected to present various aspects of the subject. Twenty minutes will be allowed to each invited speaker for the presentation of his paper. Individual members of the Congress may discuss

any one of these topics if application is made in advance in writing to the session chairman. Five minutes will be allowed for such discussions.

After the prepared discussions, free discussions will be permitted from the floor, with a limit of five minutes for each discussor.

Afternoon sessions will be arranged to permit the presentation of papers on miscellaneous subjects, which will be grouped in so far as possible according to the subject matter of the communications. Ten minutes has been allotted to the presentation of each one of these papers on miscellaneous subjects. A sufficient number of sessions will be arranged to allow for the presentation of all contributions admitted to the program by the program committee. Requests for places on the program for these ten minute papers must be submitted to the secretary of the United States committee, accompanied with abstracts in duplicate not exceeding 200 words, before Jan. 15, 1949. Only members of the Congress may submit titles to be presented during the sessions for miscellaneous communications. Each member of the Congress may present two papers. Nonmembers will be allowed to discuss presentations only if invited by the presiding officer.

The official languages in which papers may be presented are English, French, Spanish and Russian.

Membership in the Congress will consist of active and associate members. Applicants for active membership must belong to some national or local neurologic, psychiatric, neuropsychiatric or neurosurgical association or society. The fee for active membership will be \$10.

Members of families, physicians in other specialties and nonmedical persons engaged in fields of activity associated with neurology, psychiatry or neurologic surgery may apply for associate membership. The fee for associate membership will be \$5.

Application blanks for either type of membership in the Congress may be obtained by writing to the secretary of the committee for the United States, Dr. H. Houston Merritt, Montefiore Hospital, New York 67. Each application for active membership must present endorsement by some national or recognized local neuropsychiatric or neurosurgical organization or by a neurologist or psychiatrist known to members of the United States committee.

Canadian neurologists and psychiatrists interested in attending the Congress should communicate with Dr. Wilder Penfield, vice president representing Canada.

The American Express Company has been chosen as the official travel agency for the Fourth International Neurological Congress. In order to obtain the most satisfactory results, arrangements for travel or for hotel accommodations should be made through the American Express Company. Arrangements for travel may, of course, be made through any travel agency, but in order to insure the most satisfactory results it is advised that the recognized travel agency be employed for these purposes. Early application for room reservations should be made.

An effort will be made to reserve a sufficient number of various types of staterooms on some eastbound steamship sailing at the end of July or the early part of August. Similar arrangements will be made for the westbound passage during the second week in September. In all probability, special tours through various parts of France and adjacent countries will be arranged by the American Express Company for those wishing to take advantage of such facilities.

The support of the Congress will be provided by the membership fees and an appropriation from the national neurologic association of each of the constituent countries representing the equivalent of \$1 for each member of the national organization in the particular country.

The proceedings of the Congress will be published by Masson et Cie. They will consist of abstracts of presentations and discussions, together with other pertinent details concerned with the conduct of the Fourth Congress.

As no title or abstract will be accepted by the United States committee unless at the time of submission the author is an active member of the Congress, an application blank for membership properly filled out, together with check in payment of the membership fee, should precede or accompany the title and abstract and should be addressed to Dr. H. Houston Merritt, Montefiore Hospital, New York 67.

Committee for the United States Fourth International Neurological Congress

Henry Alsop Riley, chairman

H. Houston Merritt, secretary

Stanley Cobb

John F. Fulton

Foster Kennedy

S. Bernard Wortis

#### INTERNATIONAL CONGRESS ON MENTAL HEALTH

The International Congress on Mental Health, to meet in London, Aug. 11 to 21, 1948, will consist of three international conferences: (1) child psychiatry; (2) medical psychotherapy (these two conferences to run concurrently from August 11 to August 14), and (3) mental hygiene (from August 16 to August 21): Theme: Mental Health and World Citizenship. This conference will form the major part of the program and is sponsored by the International Committee for Mental Hygiene.

Membership is open to trained workers in mental health and related subjects and to members of recognized organizations connected with such work. This includes applicants in the following categories: (1) members of professional associations in psychiatry, psychology, social work, sociology and anthropology; (2) members of the medical profession, the teaching profession (including nursery school teachers), the nursing profession and the clergy; (3) members of preparatory commissions working for the conference, and (4) persons with special competence, special experience or special interest in the field of mental hygiene.

The main topics for discussion have deliberately been widely drawn, leaving preparatory commissions, 83 in the United States and 50 in other countries, and individual members freedom to select subsidiary topics (within the general framework) on which useful contributions can be made.

It is proposed to form an International Preparatory Commission with representatives from leading countries which would meet three weeks before the Congress. Its job will be to prepare a comprehensive document which would include recommendations based on the summaries of material furnished by the reports from regional discussion groups in countries all over the world. Such recommendations will be forwarded to the World Health Organization and UNESCO.

In the mornings there will be plenary sessions, with two main speakers—one chosen from the International Preparatory Commission and the other from a country at large because of his prominence in one of the professions represented at the Congress. There will be two discussants and one person to sum up, the latter to act as an alternate for either of the two main speakers if they have to drop out at the last minute. The afternoon sessions will be mainly multiprofessional, multinational small groups, which will meet to discuss the document prepared by the International Preparatory Commission. In addition, there will be

opportunity for meetings of representatives of professions, such as psychologists and sociologists. There will also be a number of small meetings, some of which may be organized by individual professions for the presentation of individual papers. At the final plenary session the document prepared by the International Preparatory Commission, copies of which will have been placed in the hands of every member of the conference, will be brought up for final adoption, with such changes as seem indicated.

A twelve man executive committee of the International Committee for Mental Hygiene, 1790 Broadway, New York 19, is coordinating activities in the United States. All inquiries should be addressed to the executive officer: Dr. Nina Ridenour, from whom further information can be obtained.

Dr. John R. Rees, of London, chief psychiatric consultant to the British army, is president of the Congress.

It is proposed to form a continuing organization out of the Congress, to be known as the World Federation for Mental Health. This would become the official voluntary consultative agency in the field of mental health for UNESCO and the World Health Organization.

Financial support from private companies and foundations, both here and in Britain, totaling \$100,000, has been received to date. Further funds are urgently needed to carry through a congress of this scope and magnitude, and a campaign has been started to raise an additional \$200,000 in this country. Contributions from individuals or groups will be most gratefully received. Suggestions as to sources of contributions would also be most welcome.

#### **DR. DANIEL BLAIN BECOMES MEDICAL DIRECTOR OF THE AMERICAN PSYCHIATRIC ASSOCIATION**

The officers of the American Psychiatric Association announce to the membership that Dr. Daniel Blain, at present chief of the Neuropsychiatric Division of the Veterans Administration, has accepted the invitation extended by the council to become the medical director of the Association. He assumed his new duties on Feb. 16, 1948 on a part-time basis, and he expects to devote his full time to the affairs of the association after about September 1. During the interim period he will devote the balance of this time to the Veterans Administration.

The position of medical director has been established for the purpose of making available to the members, the affiliated societies, the committees and sections of the Association and to public and private organizations interested in the field of psychiatry a full time psychiatric official of the Association. As medical director, Dr. Blain will activate policies approved by the Association and will stimulate the appropriate groups and committees of the Association to respond to the needs and demands of the Association and of its membership. He will be available to the members and to the affiliate societies as a source of information and advice. He will as well serve to effect liaison with the public and with interested groups on subjects relative to the work of the Association and to the general interests of society.

Dr. Blain will continue to reside in Washington, and may be addressed for the present at the Georgetown University Hospital, Washington, D. C.; his home 3126 Woodley Road, N. W., Washington 7, D. C., or through the office of the Association, Room 924, 9 Rockefeller Plaza, New York 20. Mr. Austin M. Davies will continue as executive secretary, with headquarters at the New York office. Eventually a permanent office in Washington will be secured for Dr. Blain.

Dr. Blain's distinguished psychiatric record and his unusual personal qualities stamp him as the ideal man for this position. The officers of the Association bespeak for him the warm support and cooperation of the entire membership.

#### GROUP FOR THE ADVANCEMENT OF PSYCHIATRY

The Group for the Advancement of Psychiatry was organized in May 1946 in Chicago by a number of members of the American Psychiatric Association in an effort to accelerate psychiatric progress by mutual study and discussion of outstanding problems, clarification of concepts and the determination of psychiatric needs and concrete steps required to meet those needs. The Group now has 126 members from the United States and Canada, all of whom are also members of the American Psychiatric Association. Dr. William C. Menninger, of Topeka, Kan., is its chairman, and Dr. Henry Brosin, of Chicago, its secretary. Activities of the Group are financed in part by a grant from the Commonwealth Fund.

The first formal meeting of the Group for the Advancement of Psychiatry was held Nov. 4 to 6, 1946, in Rye, N. Y., where the main subject of study and discussion was the problem of psychiatry in medical education. The second formal meeting, held at Minneapolis, June 30 to July 2, 1947, was devoted principally to the subject of state mental hospitals.

The Group comprises fifteen committees, covering medical education, research, preventive psychiatry, therapy, public education, social work, cooperation with federal agencies, cooperation with lay groups, state hospitals, racial and social problems, clinical psychology, industrial psychiatry, forensic psychiatry, international relations and child psychiatry. More than twenty experts in other fields have been invited to serve as consultants.

From time to time, the Group has adopted reports and resolutions on some of the subjects studied by its committees. A number of these reports will be published in the near future in several professional journals.

#### RESIDENT TRAINING PROGRAM IN PSYCHIATRY

Dr. Wilbur R. Miller, head of the department of psychiatry, State University of Iowa College of Medicine, and director of the Iowa State Psychopathic Hospital, announces that a new resident training program in psychiatry, organized by Paul E. Huston, M.D., assistant professor in the department of psychiatry, will be in effect July 1, 1948. This program is designed primarily to meet two objectives: to train physicians for the practice of psychiatry as a specialty and to train teachers and research workers in the field of psychiatry. A plan of supervised clinical experience and didactic courses has been arranged. The clinical experience includes rotation through the inpatient and outpatient services (both adult and children) of the Psychopathic Hospital, the psychosomatic service of the University Hospitals and the University student health service. The didactic courses will be given by members of the staff of the department of psychiatry and of the departments of anatomy, neurology, child welfare, psychology and sociology. A group of elective courses from the University and the College of Medicine are also available to meet the individual needs and interest of the participants. Candidates who complete the program and who write an accepted research dissertation will be awarded the degree of Master of Science in Psychiatry by the Graduate College.

Ordinarily, the instruction will cover a period of three years, but physicians who wish shorter periods of training, or who do not desire to become candidates for the degree, may make special arrangements. Information concerning the details of the program may be secured from P. E. Huston, M.D., Iowa State Psychopathic Hospital, Iowa City.

**NEW VIENNESE JOURNAL FOR NERVOUS DISEASES**

The first number of *Wiener Zeitschrift für Nervenheilkunde und deren Grenzgebiete* (Viennese Journal for the Treatment of Nervous Diseases and Related Subjects) will soon be published as a continuation of the *Jahrbücher für Psychiatrie und Neurologie*, which appeared until 1938.

The new journal will publish articles in all fields of psychiatry, medical psychology, neurology, pathology of the brain and neurosurgery; but, as its title indicates, other branches of medicine, the natural sciences and arts will be covered so far as they are particularly related to the wide scope of our discipline. For the present the journal will appear quarterly.

Case work will be considered only when it covers entirely fresh ground or furnishes a new point of view. The new journal aims primarily at international cooperation, which is of such great importance, especially in this branch of medicine, in which progress is at present so rapid; and it should be considered a good omen that a new impulse in this direction comes from Vienna, to whose school psychiatry and neurology owe so much in fundamental knowledge. Therefore original papers will be accepted in other world languages besides German.

The first number includes contributions from various Viennese authors, among them Berze, Holzer, Kauders, Pilcz, Stransky and Straussler.

Manuscripts should be addressed to: *Wiener Zeitschrift für Nervenheilkunde und deren Grenzgebiete*, Herausgeber Prof. Dr. Otto Kauders, Vorstand der Psychiatrisch-neurologischen Universitätsklinik, Wien IX, Lazarettgasse 14 (Austria).

**ANNOUNCEMENT OF FELLOWSHIPS FOR TRAINING IN  
CHILD GUIDANCE CLINIC PSYCHIATRY**

The American Association of Psychiatric Clinics for Children offers fellowships for training in child guidance clinic psychiatry under the auspices of the United States Public Health Service, The Commonwealth Fund and some local funds. The training is for positions in community clinics where psychiatrists, psychologists, social workers and others collaborate in the treatment of children with emotional or mental illness.

Most of the fellowships are for two years; some for one. The stipend is \$3,000 for the first year and more for the second year. Prerequisites are graduation from an approved medical school, a general internship and two years of general psychiatry.

Opportunity is provided for the fellow to develop his own skills in a well organized outpatient service with the support of a carefully planned training program and adequate supervision. The training centers are selected on the basis of standards which have been established by the American Association of Psychiatric Clinics for Children, and the fellowships are awarded by a committee of this organization.

For further information, write to Dr. A. Z. Barhash, executive assistant, the American Association of Psychiatric Clinics for Children, 1790 Broadway, New York 19.

**RESEARCH POSITIONS AT AIR UNIVERSITY SCHOOL OF  
AVIATION MEDICINE, RANDOLPH FIELD, TEXAS**

The Air University School of Aviation Medicine, Randolph Field, Texas, is in receipt of an announcement from Headquarters, United States Air Force, that the school has been allotted one of the limited number of special research posi-

tions recently authorized by Congress to attract outstanding scientists to service laboratories. This action by the Air Force is the first of a series designed to create an Air Force Aeromedical Center capable of fulfilling the needs of that force which emerged from the war as the nation's first line of defense. It is the intention of the School of Aviation Medicine to utilize the new allocation, which carries with it a salary of \$10,000 to \$15,000 per annum, to establish a civilian position vacancy for a director of research. Inquiries concerning this vacancy should be addressed to the Commandant.

#### **RESIDENCIES IN PSYCHIATRY, VETERANS ADMINISTRATION HOSPITAL, ROANOKE, VA.**

Residencies in psychiatry are now available at the Veterans Administration Hospital, Roanoke, Va.

Training will be given at the hospital under the supervision of the department of psychiatry, University of Virginia Department of Medicine. A three year program has been approved by the American Medical Association and will include didactic and clinical instruction in all phases of psychiatry and basic neurology. Residents will also actively participate in methods and technics of treating psychiatric patients.

Applications should be addressed to the manager, Veterans Administration Hospital, Roanoke 17, Va.

#### **NATIONAL INSTITUTE OF PSYCHODRAMA**

The Sociometric Institute of Beacon, N. Y., and New York city have organized seminars for the teaching and training of students, covering the fields of psychodrama, sociodrama, sociometry, group psychotherapy and other action methods as they apply to education, child guidance, adolescent deviation, intercultural relations, family and marriage problems, political and labor conflicts and community and religious problems.

The summer seminars begin June 1 and last until October 31. The training course is divided into special seminars, each lasting four weeks. For further information write to: Moreno Clinic, Beacon, N. Y.

#### **FELLOWSHIP IN CHILD PSYCHIATRY OFFERED BY CATHOLIC UNIVERSITY, WASHINGTON, D. C.**

The Child Center of the Department of Psychology and Psychiatry, Catholic University, Washington, D. C., announces a fellowship in child psychiatry for physicians who have completed one year of internship and one year of psychiatric training under supervision approved for the American Board of Psychiatry and Neurology. Further information may be secured from the director, Child Center, Catholic University, Washington, D. C.

#### **DR. A. E. BENNETT, AFFILIATED WITH THE HERRICK MEMORIAL HOSPITAL**

Dr. A. E. Bennett, of Omaha, recently resigned as professor and chairman of the department of neuropsychiatry, University of Nebraska College of Medicine. Dr. Bennett has become affiliated with the Herrick Memorial Hospital, of Berkeley, Calif., which opened a new forty bed psychiatric department in March. He took with him his professional and psychiatric nursing staff.

## Obituaries

ABRAHAM ARDEN BRILL, M.D.

1874-1948

With the death of A. A. Brill, on May 2, there passed the last of the pioneers of American psychoanalysis. He was the hardest of a hardy, devoted little group of men who fought, at first against unbelievable odds, to establish psychoanalysis as a true branch of medical science. It proved to be more than that, for nothing else that has come out of medicine has ever so profoundly influenced human thought in many fields—psychology, philosophy, sociology, art and literature.

The story of Brill's life is a typical American one—almost of the Horatio Alger sort. He was born in Kanczuga, Austria, on October 12, 1874. At 13 years of age he came to this country alone, a penniless boy, with little or no knowledge of English, but with a stubborn determination to get ahead that lasted all his life. Always he had to work for his living, but he finished high school, was graduated from New York University (Ph.B.) in 1901 and from the College of Physicians and Surgeons (Columbia University) in 1903.

After graduation he joined the staff of the New York State Hospital at Central Islip, where he organized one of the first pathologic laboratories in the New York state hospital service. By 1907 he had decided on psychiatry as his life's field; so he returned to Europe, where every one went in those days, to carry on his psychiatric education. He went first to Burghoelzli, in Zurich, where he worked under Bleuler. There he met Carl Jung, who interested him so in psychoanalysis that he went on to Vienna to study under Sigmund Freud.

When Brill returned to this country, in 1908, he was an enthusiastic psychoanalyst. Then began the long, uphill fight to establish the theory he knew to be true. A tireless worker with an enormous fund of energy, he set about to acquaint this country with Freud's discoveries. He translated many of Freud's books and articles and wrote his own in a steady stream that continued until shortly before his death. The shocked opposition he met at first among members of the medical profession would have disheartened a man of ordinary de-

termination. But Brill fought on against a stubborn opposition that did not even begin to lessen for at least twelve years. Even then the process of relenting was painfully slow and gradual, but Brill lived to see his ideas prevail. Gradually he began to be recognized as a psychiatric scientist, as more and more medical schools opened their doors to him as a lecturer. The recognition he valued as highly as any came to him in 1943, when the New York Neurological Society elected him its president—the first psychoanalyst to hold that position.

During the first world war he joined the Army Medical Corps, where mostly he taught psychiatry. During the second war he served as consultant in psychiatry at the selective service induction center in New York. During the interval, he served at the Veterans Hospital as psychiatric consultant and in a like capacity to many other hospitals around New York city. He was a founder of the New York Psychoanalytic Society and the American Psychoanalytic Association. He had been president, and later was honorary president, of both organizations. Among his other societies was the American Psychiatric Association, the American Psychopathological Association, the New York Psychiatric Society and the Society for Clinical Psychiatry, the last of which he served two terms as president. Of his books and translations, twelve were published. His articles on psychiatry and psychoanalysis make up a formidable list. In 1908 he married Dr. K. Rose Owen, who together with a son and daughter, survives.

Brill was a strong influence in the scientific field of American medicine and also in the general cultural life of this country. He had an encyclopedic sort of memory, and he was well versed in Greek and Latin, as well as the more recent literature. Many of us relied on him for quotations, especially from the classics. He was a true friend, and above all he was a good doctor.

LOUIS CASAMAJOR, M. D.

## Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND  
PSYCHIATRY, AND THE NEW YORK NEUROLOGICAL SOCIETY

Angus M. Frantz, *Chairman, Section of Neurology and Psychiatry, Presiding  
Joint Meeting, Nov. 12, 1946*

### New Anticonvulsants. DR. H. HOUSTON MERRITT.

Over seven hundred chemical compounds have been tested for anticonvulsant activity in animals. Approximately 10 per cent of these demonstrated a high degree of anticonvulsant activity in these tests.

A few of the compounds which were effective in animal tests have been given a clinical trial in patients with convulsive seizures. A brief report was given on the results obtained in the clinical use of the following compounds: 5,5-diphenylhydantoinate sodium (diphenylhydantoin sodium U. S. P.); 5-methyl-5-phenylhydantoin; 5-isopropoxymethyl-5-phenylhydantoin; 5, 5-diphenylenehydantoin, and ethylphenylsulfone.

One of the above named compounds, diphenylhydantoin, has proved to be the most effective anticonvulsant yet discovered. The results obtained with the other compounds have not been superior to those with this drug, with the possible exception of 5-methyl-5-phenylhydantoin. The latter compound has not as yet been found suitable for general use on account of its toxic side effects.

Additional chemical compounds are being tested for their anticonvulsant activity in animals and a clinical study of a larger number of those compounds which have an anticonvulsant activity in animals is in progress.

This paper, with Dr. Charles Brenner as co-author, was published in full in the May 1947 *Bulletin of the New York Academy of Medicine*, page 292.

### DISCUSSION

DR. HEINRICH WAELSCH: Dr. Merritt has given us an impressive example of the use of screening methods for testing drugs in animals, followed by the clinical trial of the drug found active by the screening method. I think this is one of the more successful screening methods, and its introduction by Dr. Merritt and Dr. Putnam has no doubt inaugurated a new era in the systematic search for anticonvulsant drugs. As Dr. Merritt has pointed out, this method seems to be useful chiefly for finding drugs effective against grand mal seizures. I wonder whether the method recently introduced by Goodman, giving subconvulsant doses of "metrazol" pentamethylenetetrazol to animals and taking electroencephalogram as a criterion, is acceptable as a test for drugs effective against petit mal, and whether Dr. Merritt has any experience with this method. Dr. Merritt has found that trimethadione ("tridione") is ineffective as tested with his method. Diphenylhydantoin sodium U. S. P. would not have been found an effective drug if it had been tested with metrazol convulsions. Of course, we, as biochemists, are to blame in that we know so little about the intrinsic mechanism connected with the pathologic situation in convulsions, and that there are no screening methods

available which affect this mechanism directly. I suppose that in the future, by a study of the intermediary metabolism, there may be found methods which will indicate which drugs may be useful in correcting the pathologic situation.

It is interesting for a chemist to speculate on the groups which are responsible for the activity of these drugs; in looking over the drugs shown to be effective in Dr. Merritt's screening test, one would conclude that the side chain has to do with the solubility and the fate of the drug in the body and determines whether the drug in effective amounts goes to and accumulates in the central nervous system. Many of these drugs are practically insoluble in water and may, therefore, be stored in the central nervous system, which is rich in lipids. In looking at the ring structure, I wonder whether the potential CO and SO groupings, which occur repeatedly in anticonvulsant drugs, have not something fundamental to do with the anticonvulsant activity.

Dr. Merritt pointed out that there are limitations to the use of many of these drugs because of their toxic action. This may indicate a failing or a decreasing mechanism of detoxication in the body. Are there indications that nutritional influences can change the situation?

Fascinating, and of basic importance, is the question of resistance to drugs. Dr. Merritt pointed out that the drugs which have been tested other than diphenylhydantoin have not received a fair trial because they were tested on patients who were resistant to the latter. I wonder whether one can formulate a pattern of resistance to certain drugs for certain groups of patients. Such a study, together with studies on twins, might indicate whether resistance to drugs has a constitutional basis, determined partly by genetic factors.

DR. CHARLES BRENNER: It is important to realize that Dr. Merritt's conclusions, which he presented so modestly, are the result of ten years of constant and unremitting effort, and that the practical effect of that effort has been great indeed. There are many thousands of epileptic patients who are now active and working in this country and abroad who would be helpless invalids without the medications which he developed in his researches.

The most striking thing about his method, it seems to me, is the simplicity of determining whether or not a drug is likely to prove of value. The initial screening process, as Dr. Waelsch said, is extremely simple, and with it one can make a survey of many drugs in a comparatively short time. Of course, this is but the beginning of the tasks, since, after one has decided whether a drug has any value in an acute experiment, the laborious tasks still remain of deciding whether it is suitable for use in human subjects and of testing it in a large series of patients with seizures. The perfect anticonvulsant drug has yet to be found, but that is the compound which Dr. Merritt is working toward, and which we all hope he will soon discover.

One of the slides which Dr. Merritt showed is important to physicians who treat epilepsy clinically. It illustrated the experiment in which a daily dose of 5-isopropoxymethyl-5-phenylhydantoin was administered to an animal with consequent elevation of the animal's convulsive threshold. I wish to emphasize that the protective effect of the anticonvulsant drug, was proportional to the size of the daily dose. The same thing is true of patients with convulsive seizures; the protection afforded them by the medication is proportional to the amount of the drug ingested. The commonest mistake in the treatment of these patients is to give the patient too small a dose for effective control of his seizures. As long as a patient is having seizures, the dose of the anticonvulsant he is receiving should be increased steadily until toxic symptoms (ataxia or blurred vision) develop.

DR. H. HOUSTON MERRITT: I wish to thank Dr. Waelsch and Dr. Brenner for their discussion. Dr. Waelsch mentioned an interesting point. If Dr. Brenner and I had used "metrazol" as our test method, we should have discarded diphenylhydantoin because this drug does not protect against "metrazol" in an acute experiment. If diphenylhydantoin sodium is given over a period of days, it will protect against "metrazol," but in a single acute experiment it will not.

With regard to an experimental method of determining the value of drugs for petit mal attacks, it is unlikely that such a method will be found, for one cannot produce seizures in animals that are similar to petit mal attacks in man.

Dr. Waelsch discussed the chemical configuration of anticonvulsant drugs. Time does not permit me to discuss this interesting subject. I do not believe that our studies enable us to draw any definite conclusions. There is, however, a great deal in what he has said about the value of the CO or the SO radical, one of which is to be found in practically all the compounds I have mentioned. As Dr. Waelsch says, the main importance of the side chain is in regard to solubility and absorption.

Dr. Waelsch spoke also of the types of drug resistance; that, too, is important. It is probably true that too much attention has been concentrated on the hydantoin derivatives. It is possible that the patients who are not helped by diphenylhydantoin will be refractory to the other hydantoins. This is not entirely true, for 5-methyl-5-phenylhydantoin helped a number of patients who were not benefited by diphenylhydantoin. It is possible that the perfect anticonvulsant will have an entirely different chemical configuration from that of the hydantoins or the barbiturates. We are working with other compounds, not of the hydantoin or the barbituric acid series, and we hope one of these will be the answer to our problem.

**Effect of Analgesics on the Intensity of Pain Experienced (Preliminary Report).** DR. JAMES D. HARDY, DR. HAROLD G. WOLFF and MISS HELEN GOODELL.

Ability to discriminate between small differences in intensity of painful stimuli was studied in 3 subjects with the pain threshold apparatus of Hardy, Wolff and Goodell. It was found that with stimuli of intensities ranging from the pain threshold to 45 per cent above this threshold it was possible to distinguish differences in intensity of  $\pm$  5 per cent of the threshold. As the intensity of the painful stimulus was further increased, this keen discrimination diminished in these 3 subjects until with intensities more than twice that of the pain threshold differentiation was no longer possible. This observation suggests that perception of differences in intensity of painful stimuli has an upper limit at approximately twice the intensity of stimulus at the pain threshold. With this and with higher intensities of stimulus, tissue damage occurred.

DISCUSSION

DR. E. CHARLES KUNKLE: These studies are of considerable clinical interest as indicating a technic of potential value in the study of an important symptom of disease. As Dr. Hardy indicated, it is also true that his experiments illustrate well the more or less roundabout development of the understanding of pain. Early investigators were particularly interested in the question of the spread of pain and of referred pain, which are secondary matters. Later, attention was paid to the question of tissues from which pain arises and the qualities of pain unique to certain tissues. Lewis and his group, in England, were particularly concerned with this aspect of the problem. Only in the past decade, since new tools have become available for the measurement of the threshold and intensity of pain, has any basic progress been made. Up to this point most physicians have been guided in their evaluation of the symptom of pain in their patients by the verbal description

of pain and by the patient's reaction to it; but these being untrustworthy evidences of the intensity of pain, Dr. Hardy and his associates have repeatedly stressed that reaction to pain is a measure of the patient's temperament or attitudes rather than of actual intensity of pain.

It is common belief that a neurotic person commonly overevaluates the intensity of whatever pain he may have. If the authors' technic can be of value as applied to such a patient, it may be possible to reeducate him with regard to the actual intensity of what he may consider an excessive amount of distress. I suspect, however, that this method as applied to such a subject may be difficult, especially when his symptom has for him a special significance, and that a symbolic one. Has Dr. Hardy had an opportunity to apply this method of estimation of the intensity of pain in so-called neurotic patients?

DR. HARRY GOLD: From one standpoint, works on analgesic agents represents the most unsatisfactory part of the field of pharmacology. From beginning to end, the investigation of these compounds has been a study in toxicology. Something has been learned about all the properties of these compounds except their power to relieve pain. A suitable method of comparing analgesic properties on a quantitative basis has not been available. Investigation of many important problems has been crippled for want of a suitable method. To mention only a few:

1. Several years ago the Committee on Narcotic Addiction of the National Research Council had before it the problem of synthetic substitutes for morphine. The pharmacologic comparisons of these compounds were extensive, but the methods of comparison led to information on various of their actions, with little, or nothing, about their relative analgesic effects.

2. Scores of analgesic agents, thrive in commerce, to one's utter bewilderment. Are they, or are they not, more effective than such simple agents as acetylsalicylic acid?

3. Several years ago a development was promoted by the pharmacologist Strakenstein, of Prague. There resulted a series of mixtures of aminopyrine and barbital; the well known preparation "allonal", each tablet contains 0.165 Gm. "alyurate" [allylisopropylbarbituric acid] and 0.097 Gm. aminopyrine) was one of them. Major claims of superior analgesic properties were made. Were these drugs superior or not?

4. There are always new mixtures of such compounds as aminopyrine, acetanilid, acetylsalicylic acid and caffeine. Is there a summation of their effects? It is well known that the action of two drugs exerting similar effects is not necessarily a functional summation. In some cases, 2 and 2 make 4; in other cases, the sum is less or more than 4.

Little is known about how these matters stood until Drs. Wolff and Hardy and Miss Goodell went to work on them by means of the method of threshold measurements of pain perception in man. Among the various revelations of these studies were the observations that analgesic agents show an increase in the pain threshold with an increase in dose but that a ceiling is soon reached, beyond which increase in the dose causes no further increase in analgesia; that the ceiling differs for different compounds, and that of a mixture of compounds in ceiling doses, the effect obtained is not the summation of the effects but the effect of the compound with the highest ceiling.

Of great importance was the fact which these investigators, emphasized, namely, that the experience of pain represents a composite of perception and reaction to pain and that the relief of pain may be only partly the result of an increased threshold; as in the case of morphine, the major part may be the effect of the drug on the mood or the psychic reaction to pain.

The present extension of their study to the effect of analgesics on the intensity of pain experienced in the range above the threshold is indeed welcome. It is important to know that a subject's judgment of the intensity of pain can be so accurately graded and that the results are reproducible with such precision. Judgment of intensity of pain brings us much closer to the problem of experience of pain as it is encountered in everyday life.

From the pharmacologic standpoint, I am particularly interested in Dr. Hardy's emphasis on the need of calibration of the subject's responses in relation to the intensity of the stimuli. The authors are essentially concerned with a problem of bioassay in human subjects, a method for the comparison of analgesic agents in man. It is a common fault in such comparisons on human subjects that a dose-response curve is not determined. The result is that two compounds of widely different potencies fail to reveal their differences because they are tested in an intensive part of the curve, in an area of the curve of response in which discrimination is lost. As I have stated, such calibration is oftenest omitted in clinical comparisons of drugs.

Does Dr. Hardy believe that the psychic reaction to pain is more intimately involved in the subject's judgment of intensity than it is in the threshold type of experiment? More specifically, if a subject were to declare that compound A and compound B were of equal potency in a test of their effects of intensity of pain above the threshold, might that subject still prefer A over B by reason of his awareness of a qualitative difference in the analgesic experience, a difference which might arise as to the result of the different effects of the two compounds on the psychic reaction to pain?

DR. JAMES F. McDONALD: This work is an interesting contribution to the physiology of sensation. The older physiology, as applied to the modalities covered in the so-called psychophysical law of Weber and Fechner, held that equal increments of stimulation produced progressively diminishing increments of sensation and that, to obtain equal increments of sensation, increasing increments of stimulation are necessary. According to Dr. Hardy's work, equal increments of stimulation produce equal increments of sensation, within the limits of tissue integrity. Here the graphic representation of sensation is a straight line, and not a line representing a logarithmic curve, as in the older formulation (Howell, W. H.: *A Textbook of Physiology*, ed. 14, Philadelphia, W. B. Saunders Company, 1940, p. 263).

In passing one might note an interesting aspect of sensation, namely, the widely different responses of different people to equal stimuli, particularly to painful stimuli. After a pyelogram has been performed on one patient, he will walk out of the office with no complaint at all, while another patient, after being subjected to the same process, may require hospital treatment with sitz bath and a hypodermic of morphine, whereas neither patient could be called neurotic. Again, a dentist finds that some patients make a big fuss over having a tooth drilled for filling, while others are bothered little by this process. I wonder whether Dr. Hardy has something to say on this point.

DR. JAMES D. HARDY: It is obvious that one cannot get far with 3 subjects, and this is a report on only 3 subjects. In the meantime, we have been testing the entire sophomore class of Cornell Medical College, and we have demonstrated that there is a small group of students (5 per cent) who, after having received a standard pain, which we graded 8+, and having been asked to fractionate the rest of the pain scale, invariably reported a painful stimulus of 1+ intensity to be of intensity of about the 5+ or 6+. We thought there must be something in the

background of these students to account for this; and, indeed, without too much probing, it was easy to bring it out. Two of the students had had amputations, and they had a definite orientation toward the pain experience. As one of them said, nothing he received in any of the stimuli "really hurt him." Two or three other students said they were not insensitive to pain. It may be considered remarkable that the pain thresholds of all of the students were in the normal range.

In response to Dr. Gold's question concerning the effectiveness of analgesic A, as compared with that of analgesic B: It is apparent from our studies that the side effects of the agent are important in affecting the person's attitude toward the pain experience rather than the analgesic property of the agent. It is probable, therefore, that the agent which relieves the patient's anxiety is more to be desired.

#### PHILADELPHIA NEUROLOGICAL SOCIETY

Robert A. Groff, M.D.

*Regular Meeting, Nov. 22, 1946*

**Myasthenia Gravis in a 9 Year Old Boy.** DR. EDWARD T. TRONCELLITI (by invitation).

Myasthenia gravis in patients under 17 years of age is rare. My colleagues and I have been able to collect reports of only 37 cases in the literature of this disorder in children under 17 years of age. The disease was first described by Willis in 1872 and was recognized by Erb as a clinical entity in 1878. However, the first report of the disorder in a child was made by Remak in 1892, the condition occurring in a 12 year old girl. In a series of 34 cases in patients under 17 years of age, Levethan and associates found the average age to be 11.8 years, and there were only 8 patients under 10 years of age. Strictroot and associates reported a case in a newborn infant of a myasthenic mother, and Kawaichi reported a case in a 21 month old infant. There have been no other actual reports in the literature of cases of myasthenia gravis in children. Because of the infrequency, if not rarity, of the occurrence of this disease, we believe it is of interest to the medical profession to report this case and to comment on the effectiveness of the therapy thus far carried on.

#### REPORT OF A CASE

A white boy, 9 years and 2 months of age, was admitted to the Mary J. Drexel Children's Hospital on June 9, 1946, for study. The chief complaint on admission was that of ptosis of both eyelids of three months' duration. A ptosis of the left eyelid was first noted in March 1946. The ptosis became more marked and about two weeks after its appearance the eye was almost closed. The ptosis of the left eye improved somewhat. However, the same difficulty began on the right. Since then the ptosis of the right eye had become progressively worse, and was more marked at night than in the daytime. The patient also complained of diplopia in the inferior field of vision. He became fatigued easily and was unable to play as actively as the other children of his own age. There was also a history of difficulty in breathing for about one year prior to admission. However, no complaints referable to mastication were obtained. The child had been seen by his family physician during the past three months and had also been studied at one of the ophthalmologic hospitals in this city. He was to have been fitted with lenses at the time he was referred to our hospital for study.

Physical examination on admission revealed a somewhat obese young boy, weighing 84 pounds (38.1 Kg.), alert and cooperative and in no distress. There was

present a bilateral ptosis, more marked on the right lid. The pupils were somewhat dilated but reacted to light. There was no lessening of the response to this test after ten attempts. The external ocular movements were normal. There was ptosis of the left lid, and the right was almost completely closed. The child complained of double vision in the inferior fields. The fundoscopic examination was normal. The remainder of the physical and neurologic examination gave negative results except for a slight posterior cervical adenitis.

Laboratory studies, including urinalysis, complete blood count, serologic examination of the blood, and tuberculin patch test, all gave negative results. The glucose tolerance curve was normal. A roentgen examination of the chest showed no evidence of thymic enlargement, and the upper part of the mediastinum was normal in appearance. The ophthalmologic consultation confirmed the diplopia in the inferior fields, and the ptosis, and it was noted that the left eye deviated laterally under cover.

*Course in the Hospital.*—During the three days following admission, it was noted that the ptosis was less marked in the morning than at night. The child was fairly active about the ward. On June 13 (four days after admission) the child was given 0.3 Gm. of quinine sulfate twice, at a two hour interval. In two hours the ptosis was more marked, and he complained of his arms being tired and heavy and feeling sleepy. When the patient was asked to count to 100 he frequently had to stop and had difficulty in speaking. He also complained of difficulty in breathing and there was a flatness of the muscles of expression. He was then given 1 mg. (2 cc. of 1:2,000) "prostigmine methylsulfate" U.S.P. (neostigmine methylsulfate) intramuscularly. In twenty minutes the ptosis had disappeared as had also the tired and heavy feeling in his arms and his sleepiness. He was able to count to 100 without difficulty. This same test was tried once more, isotonic sodium chloride solution given intramuscularly being substituted for "prostigmine methylsulfate" to rule out definitely a psychogenic factor. No response was noted. The child's treatment was standardized at a dose of 15 mg. of "prostigmine bromide" four times daily and 8 mg. of ephedrine sulfate twice daily and he was then discharged from the hospital on June 24.

Since being discharged from the hospital, the child has been followed closely as an outpatient. He was maintained on 15 mg. of "prostigmine" orally four times daily and 8 mg. of ephedrine sulfate twice daily. He spent the entire summer from July 1 to September 1, 1946, at a seashore resort. He was seen once weekly and was able to carry on without difficulty. The ptosis was never noticed, and he was able to run and play on the beach the entire summer without difficulty. On his return to the city he was less obese and more muscular than on discharge from the hospital. He returned to school and plays with his classmates constantly. He has been maintained on 15 mg. of "prostigmine bromide" three times daily, and he no longer requires the ephedrine sulfate. Another roentgen examination was made during the past month, and no evidence of thymic enlargement was noted.

It has not been found necessary to readmit the child for a further period of hospitalization, as he has been symptomless since being discharged five months ago.

*Comment.*—In the pediatric and neurologic literature no review of the condition in children can be found except that of Levethan and associates. The onset of symptoms in most cases of the disease is insidious, as reported by these authors. In 19 per cent of the cases the first complaints were fatigability and general muscular weakness. Symptoms such as ptosis and diplopia, as in our case, were presenting symptoms in 17 per cent. Disturbances of speech and of deglutition were found to be late symptoms. In 21 of 34 cases, involvement of speech was present at

some time during the course of the disease, but it was the presenting symptom in only 5 cases. Dysphagia occurred at some time in 20 cases and initially in 3.

Enlargement of the thymus, which has been considered to be associated frequently with myasthenia gravis, was reported in but 1 case by Booth. Roentgen studies in 6 cases, including ours, and postmortem examinations in another 5 cases failed to reveal thymic enlargement or any constant pathologic change. Milhorat, Wolff and Adams, Power and Boothby express agreement that the changes in cases of myasthenia gravis are not uniform.

Although there is little in the literature concerning the use of the "prostigmine" compounds for children with myasthenia gravis, their use for this disease is well established. Viets and Schwab analyzed their experience in administering "prostigmine" to 44 adult patients and state that "prostigmine bromide" taken by mouth and supplemented with ephedrine sulfate, potassium chloride and occasionally guanidine, is the most efficient form of therapy now available.

Eaton describes the diagnostic test for myasthenia gravis with "prostigmine methylsulfate" and quinine sulfate which was used by us in this case. Bennett and Cash describe a test and a new approach to causation of the disease with curare.

Thymectomy has been prescribed by many when there is evidence of thymic enlargement. Blalock, Campbell and Poer, all report cases with remission following thymectomy. Aring reported cases in 3 adult women, of whom 2 had thymic enlargement, who were treated with radiation with excellent results while in the third case no enlargement was found and less response was noted.

Total duration of the disease in our case has been about seventeen months until the date of this report. The average duration of the 37 previous cases was forty-four months. In 13 cases in children under 12 years of age the average duration was fifteen months, and in 10 cases with fatal termination of the disease it was 15.6 months.

We have purposely not attempted to discuss the chemical findings and the causation in this disease, as there is no agreement in opinion by the workers in this field.

#### DISCUSSION

DR. CHARLES RUPP: I think the interesting feature in this case is the occurrence of myasthenia in so young a child. Personally I have never seen a case at so young an age.

I have seen this youngster on a number of occasions and feel there is no question concerning the diagnosis. The first time I saw the child was early in the morning and there was no objective evidence to substantiate Dr. Troncelliti's diagnosis, but the next day when I saw him in the afternoon there was no doubt about the ptosis. The prognosis interests me. According to what Dr. Troncelliti tells us this child already has lived longer than one would anticipate. In speaking to some of my older colleagues regarding this case, several said that it was their impression that when myasthenia occurs in childhood a prognosis may be more favorable than when the onset is delayed until later in life.

DR. JOSEPH C. YASKIN: Mr. President, what was the strength of the orbicularis oculi in this case?

DR. EDWARD A. TRONCELLITI: As far as we could tell, it seemed to be normal until the time that we gave the quinine sulfate. He seemed to be able to raise the eyelid without difficulty. Then after receiving the quinine he could not, and he would have to raise his eyebrow to get his eyelid up.

DR. JOSEPH C. YASKIN: It is not a question of raising the eyebrow; the orbicularis oculi closes the eye. I have yet to find a case in the last ten or twelve years

of myasthenia gravis with ocular signs which does not have a constant weakness of the orbicularis oculi. In fact, this sign helped me in making a diagnosis in many doubtful cases.

At the risk of boring some of my colleagues, I might recite a case or two.

There was an operating room nurse in the Reading Hospital who had a recurring diplopia which could not be accounted for for many years, except on one occasion when she had an infection of the upper respiratory tract. In order to get her breathing apparatus working, she used ephedrine and got rid of her diplopia. On admission to Dr. Spaeth's service at the Graduate Hospital, all she had was the complaint of diplopia. In addition, she had a definite weakness of the orbicularis oculi.

I have tested many cases since, and I think I have demonstrated most of them at the clinic. Even when one gives "prostigmine" and the ptosis disappears and the diplopia disappears and the facies straighten out so they don't look like myasthenic facies, the orbicularis oculi remains weak, and I regard it as a valuable sign.

It would be of great interest, Dr. Troncelliti, when the child comes to your clinic next time, to tell him to close the eyes tightly and then to try to open them.

Another interesting thing about your presentation is the amount of "prostigmine" you use, 15 mg. four times daily. This is no criticism. It was only within the last year that I learned that I used all too little "prostigmine" for my adults.

I had a patient with marked diplopia. I prescribed the ordinary dosage and I didn't get any results. He was one of the consulting engineers for the Du Pont corporation, and not knowing what else to do with him I gave him an encephalogram and I suggested he go to Rochester. They gave him about 14 tablets a day, and he had a much better result. I learned that I wasn't giving enough "prostigmine bromide." For some reason I have a fear of this drug.

In a more recent case I had a similar experience and one of my colleagues in the north informed me again that I am not giving enough "prostigmine." So instead of giving the patient 1 tablet four times a day, I now give him 2 tablets four times a day, and it apparently makes a lot of difference. I don't know what the "prostigmine" will do when given in large doses over a long period of time. This is something I am not familiar with, but apparently those who use it do not fear it.

DR. CHARLES RUPP: In answer to Dr. Yaskin's question of the effect of large doses of "prostigmine" over a long period of time, I have under my care a woman who at times has taken as many as 20 tablets a day. She had to take a little atropine with it to counteract the effect on the gastrointestinal tract, but otherwise she seemed perfectly healthy. She had a position in one of the department stores of some responsibility and got along well.

DR. MILTON MEYERS: I think the case is remarkably well presented. I don't question the diagnosis at all, but I would like to know whether the electrical test bore it out. Did the muscles keep on responding to electricity or was there diminution?

DR. EDWARD A. TRONCELLITI: An electrical test was not done in the case.

DR. SHERMAN F. GILPIN JR.: What interests me is the giving of that much "prostigmine" to a youngster of that age without atropine.

I had a girl about 19 years old in the office one day some time ago, and without thinking much about it I gave her 1.5 mg. of "prostigmine" plus a 0.01 grain of atropine and told her to go on out for an hour and come back. About half an hour later I received a call from a nearby store saying they had the woman in their

infirmary with severe abdominal pain. Then I got to thinking about the fact that **this girl was very slightly built.** Although she was 19 years of age she weighed only about 90 pounds (40.8 Kg.) at the most. I was led to believe that I had better be a little more conservative. So when I hear about 1 mg. given to this youngster 9 years of age without atropine, I am happy because it makes me feel better about giving it to this girl.

The other thing that occurs to me is that Dr. Rupp has quoted Dr. Viets on the prognosis. It happens that the last 2 patients I have seen, 1 at Philadelphia General Hospital, whom all of you have seen, I am sure, and 1 at Temple, both patients around 65 years of age when the diagnosis was first made, are both under the sod now. The man at Philadelphia General Hospital lived about two years; the woman lived a little less than a year. The woman got what I thought were huge doses until I heard of this case. She was getting about 28 tablets per day of 15 mg. each.

As far as the toxic symptoms are concerned, Dr. Nielson has reported the development of bromidism from the administration of too much "prostigmine bromide." The woman I referred to, having received twenty-eight tablets a day, had no evidence of an accumulation of bromide in her blood.

DR. EDWARD A. TRONCELLITI: We did think of the possibility of abdominal pain and so forth in this child. As a matter of fact, the first time he was given "prostigmine" he was given atropine along with it. At the very beginning in the hospital, while we were in the trial and error stage of determining his dosage, he did have some abdominal pain. However, as we got to the dosage that we needed—first giving a lower dose and then gradually building up, we came back to a dosage of four tablets of 15 mg.—it disappeared and he has not had any abdominal pain since that time.

#### **Subacute Combined Degeneration of the Spinal Cord Occurring in Identical**

**Twins.** DR. GABRIEL A. SCHWARZ AND LIEUTENANT JOHN C. TODD, Medical Corps, Army of the United States (by invitation).

In 56 year old, white twin brothers there developed within a few years of each other weakness, ataxia and paresthesias of the extremities. Clinically, they both presented signs relatively characteristic of posterolateral sclerosis. They did not have anemia at any time, nor any indication of hyperchromia or macrocytosis. Both had achlorhydria with use of histamine. Both brothers recovered following parenteral use of liver extract.

The monozygosity of the brothers was established on the basis of identical physical characteristics, blood groups and finger and palm prints.

These cases are felt to strengthen the concept of heredity as one of the etiologic factors in the development of subacute combined degeneration of the spinal cord.

#### **DISCUSSION**

DR. JOSEPH C. YASKIN: Mr. President, were any sternal punctures made in this case? After all, the diagnosis of pernicious anemia nowadays has a much more direct approach than the blood count, the study of the gastric juice or the neurologic signs. A sternal puncture always gives positive results with pernicious anemia, unless there has been intensive treatment. Dr. Schwarz must have done those punctures before. It would be interesting to know the results.

DR. FREDERIC H. LEAVITT: This case presentation is of interest to me primarily because of the incidence in identical twins. On several occasions I have reported before the Psychiatric Society in this room concerning identical neurologic conditions occurring at about the same time in homologous twins. The first group were two homologous brothers in whom there developed at the same time midline cerebellar tumors of the medulloblastomatous type. On another occasion I reported

concerning the development of major epilepsy at the same period in proved identical twins. In these two sets of cases the palm prints and those of the soles showed identical whorls and quite similar palm and sole print patterns. One of these cases exhibited a mirrored replica of the other, and also the whorls of the hair of the scalp were mirrored replicas.

Dr. Walter Freeman reported a few years ago before the American Neurological Association several instances of neurologic disorders occurring simultaneously in identical twins.

Discussing this presentation relative to primary pernicious anemia—in my recollection it is unusual for this to be a familial affair. I remember 1 patient, a mother, who had had five children. The mother had primary pernicious anemia and a concomitant subacute combined sclerosis of the cord, and I remember she did not respond at all to the usual therapy of pernicious anemia and eventually died from the advancement of her sclerotic cord condition. In 1 of her five children, a daughter, primary pernicious anemia developed when she was in her thirties, but sclerotic cord symptoms did not develop. This daughter responded splendidly to the usual form of therapy for pernicious anemia and made a complete recovery.

DR. HELENA RIGGS: Since the use of liver treatment, so many times the possibility of posterolateral sclerosis is forgotten. At the Philadelphia General Hospital we have had 4 cases of undiagnosed disease of the cord, all of which at autopsy turned out to be posterolateral sclerosis, and pernicious anemia was confirmed by post-mortem studies of the bone marrow.

DR. GABRIEL A. SCHWARZ: As to Dr. Yaskin's question about the sternal puncture the first patient was studied at the Philadelphia Naval Hospital. No sternal puncture was done on this man there. On the patient who was studied at the University of Pennsylvania Hospital we unfortunately did not make a sternal puncture before liver therapy was used, because pneumonia developed. We started liver therapy immediately because he was so ill.

**The Spinal Fluid in Poliomyelitis.** DR. GEORGE D. GAMMON, DR. JOHN C. TODD, (by invitation), DR. PASCAL LUCCHESI (by invitation), DR. ALFRED LABOCCETTA (by invitation), DR. BURTON CHANCE, JR. (by invitation), DR. ALEXANDER SILVERSTIEN and DR. F. WILLIAM SUNDERMAN (by invitation).

The spinal fluids from 21 cases of poliomyelitis were examined at frequent intervals up to one hundred and ten days after onset. The cell count was usually normal after the first week, but occasionally reached 20 to 60 cells late in the disease.

The spinal fluid protein was elevated above 40 mg. per 100 cc. in all but 4 cases. The maximum rise occurred between the tenth and the thirty-fourth day. Normality was attained in thirty days in some cases but others remained elevated for the whole period of observation. The maximum elevation was 392 mg. per 100 cc. and half the cases were above 100 mg. This level of spinal fluid protein has led to diagnostic difficulty in relation to Guillain-Barre's syndrome and diphtheritic neuritis. No correlation with the extent of initial or residual paralysis was noted.

#### DISCUSSION

DR. SHERMAN F. GILPIN JR.: This paper to me is very interesting in that it serves to emphasize the fact that we know very little about the spinal fluid protein. At least I feel that way. I could add another condition in which the spinal fluid protein is often increased, namely, so-called diabetic polyneuropathy.

Two years ago at the meeting of the American Neurological Association in New York, there was a medical man, as I remember it, who spoke of 100 patients who were on the medical service in one of the New York Hospitals, all of whom had elevated spinal fluid proteins, and in none of whom there were any neurologic findings. It happens that at Temple University I have been upset recently because we have obtained elevated proteins in many cases for which I could see no cause. Hence, this paper is stimulating to me. Here are cases of poliomyelitis followed up a long time in which protein is elevated.

I should like to ask a question—I am interested in learning whether there are any patients with poliomyelitis who early in the disease, we will say the first few days, do not have pleocytosis.

DR. F. H. LEWEY: I was very much interested to learn that the increase of protein lasts so long.

The fact is not so unknown as Dr. Gilpin seems to believe. It has been well known for at least ten years that in virus diseases the so-called crossing of the curves occurs in the spinal fluid. In a very early phase, around the third to fifth days, there is an increase of cells to 50 or 100 with a low protein content. Later the protein increases. When I learned this from Carl Lange, about ten years ago, we studied the patients at the Children's Hospital, and verified it.

As to Dr. Gilpin's second question, this is another problem which is not unknown. All of us during our life pass through so-called virus diseases which give no more marked signs than pain in the back or headaches, and which may leave behind an increase of spinal fluid protein. Another possibility is that one of these dormant infections becomes manifest with the disease for which the patient comes to the hospital.

DR. HELENA RIGGS: We have been making quantitative studies of spinal fluid at Philadelphia General Hospital for about ten years. Dr. James Dean collected 200 cases, not from the neurologic wards, with a protein content over 40 mg. It is fairly common to find a protein increase in cases of uremia, of chronic alcoholism or even of decompensated cardiac conditions.

In acute spinal meningitis, long after the spinal fluid is sterile and there are no cells, the protein may be very high. In 1 instance it persisted for three months with no clinical signs of involvement of the nervous system. I would rather doubt that the activity of the virus could be checked on the basis of the increased spinal fluid protein.

\*CAPTAIN IRVING STERNSCHEIN (by invitation): I should like to add to Dr. Gilpin's comment. I think the 100 cases he referred to were studied by Rabiner and Apter at the Kings County Hospital, Brooklyn. They were cases of pneumonia with temperatures elevated to 103 F. or thereabouts. Practically all of the patients had elevated spinal fluid proteins, close to 100 mg. per hundred cubic centimeters.

In the service I have seen a number of cases in which there were marked elevations of protein with relatively little cellular response. These usually followed severe pharyngeal infections, occasionally diphtheria. In rare instances there were no apparent antecedent infections. These were not cases which could be classified with the Guillain-Barre syndrome. I think the term Guillain-Barre syndrome can no longer be considered a final diagnosis in all cases demonstrating an albuminocytologic dissociation.

DR. BURTON CHANCE JR.: I might say, in answer to one of the doctor's questions, that some of the cases we have seen at Municipal Hospital definitely include a number of cases of poliomyelitis that have no cell reaction at the time they are punctured shortly after the first symptoms appear.

DR. ALEXANDER SILVERSTEIN: I think we might mention that in the earliest phase of poliomyelitis the spinal fluid may show a pleocytosis of 500 or more cells with a polymorphonuclear predominance, a picture simulating meningitis. However within forty-eight hours this is changed to a lymphocytic predominance with a drop in the cell count to about 100 cells per cubic millimeter. The only other condition wherein the spinal fluid may act in this fashion is tuberculous meningitis.

As to the content of the spinal fluid protein showing a rather definite pattern in cases of poliomyelitis, we at the Philadelphia Hospital for Contagious Diseases have not been aware of this particular feature as a factor in the clinical picture. Usually in the acute phase, that is, within the first two weeks, the protein seldom rises above 100 mg., and I believe the value in Dr. Gammon's work is that he continued to study the spinal fluid protein in some of these cases much later in the disease. Thus he was able to discover a spinal fluid picture in poliomyelitis of 200 or 300 mg. of protein which we usually associate with the so-called Guillain-Barre syndrome. Usually in a polyneuritic syndrome, the persistence of a marked increase in quantitative protein spinal fluid, especially if the paralysis is bilaterally symmetric, would suggest that the particular case should be labeled as one belonging to the Guillain-Barre group. From a practical, clinical standpoint, therefore, the fact that one can obtain the same type of change in spinal fluid protein in poliomyelitis and the polyneuritic syndrome I think is worthy of emphasis and a point which deserves further study.

DR. MICHAEL SCOTT: I should like to comment about the increase in protein in cases of so-called albuminocytologic dissociation. Here a diagnosis is made of neuritic or polyneuritic syndrome and the protein is found markedly increased with no increase in white cells. The clinician must bear the burden of ruling out a space-taking lesion. This syndrome must not be confused with that due to a space-taking intraspinal lesion, and it is therefore essential that when a marked increase in protein is found that a Queckenstedt test as well as a myelogram be done.

DR. ALFRED LA BOCCETTA: The spinal fluid cell count early in poliomyelitis may not be increased. This is not often the case in the bulbar type. We have seen cases of poliomyelitis which were clinically diagnosed as poliomyelitis and in which there were normal spinal fluid cell counts. The spinal fluid cell count in poliomyelitis varies considerably from season to season and in different years.

In some outbreaks the cell count has ranged from 20 to 75 cells while in others it may range from 100 to 150 cells. Occasionally we have seen cases with counts around 475 cells, which is not usually associated with acute poliomyelitis. Although a cellular reaction is expected in poliomyelitis, we have seen cases with a normal spinal fluid cell count.

DR. GEORGE D. GAMMON: In an epidemic down in Carolina a number of years ago, there were cases in which there were no cells in the acute phase. I remember Dr. Paul commenting on that fact.

One thing that this discussion has brought out pleases me very much, and that is that it calls attention to the fact that an elevation of protein without increase in cells occurs in a number of different conditions. We have gotten into the habit in this country of diagnosing Guillain-Barre syndrome for any condition accompanied by an elevated spinal fluid protein. What we really mean is that we are diagnosing a spinal fluid syndrome, not a clinical syndrome. Guillain has always insisted that a high protein content was only one of the essential features of his syndrome. He was perfectly aware that this rise occurred in diphtheria.

You can extend the list with elevated protein—I have seen it in neuritis associated with periaarteritis nodosa. It has occurred in some alcoholic neuritic cases. You

may find it in a number of infections; in fact, in diphtheria without any peripheral neuritis. Certainly Dr. Scott is right, because we have mistaken cases of tumor for Guillain-Barre syndrome.

What we were aiming at here was to try to determine whether there was a special curve for poliomyelitis which could be compared with that of diphtheria or Guillain-Barre syndrome. So far as I know, there is only one series of cases of Guillain-Barre syndrome that have been studied serially over a long period of time, and that is a series by Van Bogaert in which he says that maximum protein content was attained between the fourth and eighth weeks and that there was often a decline to normal by the ninetieth day. He states that in poliomyelitis the rise begins and reaches a maximum between the fourteenth and fifteenth day and that it decreases around the forty-fifth day. It reaches a level of around 100 mg. In the Guillain-Barre syndrome the protein rises and reaches a maximum at a later date, between the fourth and eighth week, and then slowly declines, but the elevation is higher.

On the other hand, our curves show that in poliomyelitis there is a maximum protein content for as long as forty days; so we have the same time period of rise that Van Bogaert describes in the Guillain-Barre syndrome. I do not know of any series of cases of diphtheritic neuritis which can be compared. If any of you do, I should like very much to hear of it.

To sum up, there are many, many cases of disease with elevation of the spinal fluid protein which are not the Guillain-Barre syndrome, and personally I deplore the use of that term indiscriminately.

#### CHICAGO NEUROLOGICAL SOCIETY

Joseph A. Luhan, M.D., *Vice President, in the Chair*

Nov. 12, 1946

#### **Role of Psychosis in Amyotrophic Lateral Sclerosis: Report of Case.**

DR. JOSEPH W. FRIEDLANDER AND DR. BENJAMIN H. KESERT.

The reported coexistence of psychosis and amyotrophic lateral sclerosis is so rare that a survey of European and American literature reveals only 34 cases, and in many of these the psychosis was functional. When it occurs, however, the question arises whether the mental symptoms are secondary to the organic disease or merely coincidental.

The case reported here is that of a white coal miner aged 50, whose symptoms apparently began in August 1943, in the form of pain and paresthesia in the right lower extremity. Mental changes were noted in February 1946. On his admission to Veterans Administration Hospital at Hines, Ill., in August 1946, he was almost mute; yet it was possible to make a diagnosis of dementia from his behavior. He would "read" books upside down, tear out the pictures and stuff them in his pockets. At first he was euphoric but later became depressed. He responded only to the simplest commands and would solve all arithmetical problems presented on paper by attempting to write his name. When a cigaret was held just out of reach, he would follow it indefinitely.

Neurologic examination revealed the signs of amyotrophic lateral sclerosis, including progressive bulbar palsy. Laboratory tests revealed nothing significant except for pneumoencephalographic evidence of diffuse cerebral atrophy.

This study supplements the work of Wechsler and Davison (Amyotrophic Lateral Sclerosis with Mental Symptoms, ARCH. NEUROL. & PSYCHIAT. 27:859

[April] 1932) and of Androp (*Psychiatric Quart.* **14**:818 [Oct.] 1940), each of whom presented histopathologic data. On this basis, we suggest that an organic psychosis may play the same role in amyotrophic lateral sclerosis that it does in multiple sclerosis.

## DISCUSSION

DR. JOSEPH A. LUHAN: In looking over the necropsy material at Cook County Hospital since 1941, I found 4 cases of amyotrophic lateral sclerosis, in 3 of which there was considerable atrophy of the frontal convolutions beyond the motor cortex. Histologic examination confirmed the gross diagnosis of an atrophic process. In 2 cases aphonia prevented adequate evaluation of intellectual functions, but in the third case, that of a man aged 69, dementia developed before fatal termination of the illness. A photograph of the gross appearance of the brain, from which the meninges had not been stripped away, revealed clearly the convolutional atrophy affecting most of the frontal lobes.

**Effects of Cerebral Electric Shock on Experimental Neuroses in Cats.**

DR. JULES MASSERMAN.

During the past ten years a method has been developed of including experimental neuroses in animals by setting up an opposition of biologic needs and motivations and so creating disturbing conflicts between accustomed modes of adaptation—for instance, between the expressions of hunger and fear. In animals subjected to several such conflicts, lasting aberrations of behavior developed that might justifiably be termed experimental neuroses. In effect, the animals manifested various physiologic disturbances characteristic of severe anxiety; responded to innocuous sensory stimuli with phobic hypersensitivity, inhibition or exaggeration of reaction; showed severe disturbance of visceral and motor function, and exhibited persistent and generalized abnormalities of conduct, both in and out of the experimental situation.

The induction of these neurotic states afforded an opportunity to study various forms of therapy. These therapeutic methods consisted in prolonged removal from disturbing stimuli, forced solution of the motivational conflict, retraining by the experimenter and reexploration of the neurotogenic situation by the animal, use of rehabilitative relationships between normal and neurotic animals and, finally, use of sedative drugs, such as morphine, the barbiturates and alcohol. Alcohol, in particular, disorganized the intricate and complex aberrations that constituted an experimental neurosis and permitted previously established and simpler adaptive patterns to emerge; in this way, alcohol seemed to exert a temporary therapeutic action on neurotic behavior. In fact, some animals seemed to learn that alcohol produced these effects, thereafter sought the drug spontaneously and thereby became experimental "alcoholic addicts." The observation that drugs which disrupted cortical integration significantly affected neurotic behavior led to the work with electroshock presented here.

*Summary of Moving Picture.*—Six cats were made experimentally neurotic by being subjected to from two to seven conflicts between hunger and acute fear and were then given cerebral electroshocks equivalent to those used in clinical therapy. All the animals showed a pronounced disintegration of feeding inhibitions, signal phobias, compulsive and regressive reactions and other neurotic patterns, with emergence of simpler and more normally adaptive behavior. Their behavior could be further improved by guidance and retraining and ancillary "psychotherapeutic" procedures. Nevertheless, all the neurotic animals and 2 normal controls subjected to electroshock also showed impaired efficiency and diminished capacity

for new learning and complex readaptations. In no case could these deficits be correlated with significant histopathologic changes in the brain.

## DISCUSSION

DR. BENJAMIN BOSHES: I was glad to see this moving picture; it occurred to me that these experiments were inadvertently repeated with men at Oran, where I was stationed. In the early part of the war, the hospital was the dumping ground for patients with battle neuroses. Instead of air blasts in the experimental cage, these men had faced repeated bombing and shelling. They had had psychotherapy of every type, including hypnosis, narcosynthesis and *Dauer-schlaf*, and everything had failed. They were finally sent to our hospital. There were few hospital ships, and no shipmasters of freighters would take them. The symptoms were almost like those of Dr. Masserman's animals. The men had to be tube fed, and if given sedatives would have a recurrence of battle dreams. Many had coarse tremors; some, a wing-beating type of tremor. In desperation, my colleagues and I tried electric shock treatment. I was interested in Dr. Masserman's mention of the "four shocks," for we found that 75 per cent of our patients showed clearing of the symptoms after three shocks and the rest complete clearing of the battle-induced neurosis after four shocks. It is interesting that when we were raided by Germans and Italians, these men, who previously could not stand a snap of the fingers or the flicker of a light, went through these air raids, some with a slight upset, but with return to normal function in a few hours.

These experiences were published in the paper of this theater of operation, the *Medical Bulletin of Natoussa*; but, for reasons of security, the article was not published in the United States. However, it is available if you wish to see it.

DR. R. P. MACKAY: This beautiful piece of work confirms the observations of many of us on our clinical patients receiving shock therapy, a method of treatment which is undoubtedly one of the remarkable achievements in psychiatry in the past one hundred years. Amnesia, which varies greatly from one patient to another, is a salient feature to be observed clinically after shock therapy. It is interesting, therefore, that Dr. Masserman's cats recovered from their neuroses under shock therapy and continued to perform their conditioned reflexes without much objective evidence of "amnesia." May I inquire whether Dr. Masserman noticed any evidences of deterioration of conditioned reflexes as a result of shock therapy which might be correlated with clinical amnesia? I have enjoyed his presentation and wish only to ask, "What is Freud's place in all this?"

DR. PERCIVAL BAILEY: I wonder whether Dr. Masserman ever found a cat that would face an air blast and feed nevertheless. I am told that guinea pigs will face disagreeable stimulation to attain the goal of sexual gratification.

DR. JULES MASSERMAN: I am grateful for this discussion. I agree with Dr. Boshes, for I observed in these animals partial disintegration of recognition and recall after electroshock. If a cat taught to pass a difficult barrier and work the switch three times in a row is subjected to shock, the animal will revert to the simpler pattern of working the switch only once. So, too, after electric shock the complex behavior of patients may be disintegrated, but they do not forget to feed themselves.

I invite Dr. Bailey to come to the laboratory and observe more than one animal walk over to the switch, press it down, give itself a terrific air blast and then proceed to repeat the performance. Such "masochistic" behavior can be produced by teaching the cat to respond to the light signal for food, then to work the switch and then to tolerate increasingly severe air blasts or electric shocks to

the paws as substitutes for the light signals. After this, the animal will continue to seek these apparently traumatic stimuli even when the food reward is discontinued.

#### **A New Mechanism in the Inhibition of Certain Experimental Convulsions.**

DR. R. K. RICHARDS.

With few exceptions, chemically induced convulsions in experimental animals are usually antagonized by depressant drugs, such as anesthetics, barbiturates or bromides.

In spite of the remarkable progress in analyzing the electric and biochemical phenomena connected with convulsions or depression, little is known about the actual process involved in these phenomena. A new approach appeared possible by making use of an observation well known in chemotherapy, namely, the competitive inhibition of the bacteriostatic effects of sulfonamide drugs by the chemically related para-aminobenzoic acid.

Procaine, a potent convulsant, is a combination of para-aminobenzoic acid and diethylaminoethanol. In vivo it is readily split into two components, which are pharmacologically inert. It was shown that pretreatment with either para-aminobenzoic acid or diethylaminoethanol effectively inhibited the central convulsant action of procaine. The mixture of the two drugs was even more effective. Systematic investigation of derivatives of these two compounds revealed interesting correlations of structure and protective action. Further pharmacologic analysis makes a competitive inhibition action on the brain cells or on certain metabolic processes the most likely explanation of this new phenomenon.

Of particular interest are the restriction of this inhibiting action to nerve centers and its absence in the peripheral effects of procaine. It is not impossible that the accumulation of the split products of procaine in the body are a reason for the unexpectedly high tolerance to intravenous injection of procaine, as it is now used in the clinical investigation of the drug as a systemic analgesic and anesthetic.

#### DISCUSSION

DR. ISIDORE FINKLEMAN: How does this work compare with that of Beutner, who also produced convulsions with procaine and inhibited them with calcium chloride or calcium gluconate?

DR. R. K. RICHARDS: If one injects calcium salts mixed with procaine, as was done by Beutner and his associates, a reduction in the toxicity of procaine can be observed. This effect is largely local and is probably due to a delay in absorption of the local anesthetics, which can also be obtained by using mercurial diuretics instead of the calcium.

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Dec. 10, 1946

#### **Dissociation of Pain and Temperature Sensibility with Lesions of the Spinal Cord. DR. IRVING C. SHERMAN and DR. ALEX J. ARIEFF.**

The literature on this subject is scanty. The authors discussed the various theories of how this sensory dissociation could be produced, chiefly, those of the existence of separate tracts for each modality and the greater vulnerability to damage of one type of fiber over another.

Three cases of dissociation of pain and temperature sense accompanying intramedullary or extramedullary disease of the spinal cord were reported. In the first case, that of syringomyelia, temperature sense was present but diminished in areas of analgesia in two separate dermatomes. In the second case, that of an intramedul-

lary lesion of undetermined cause, there was loss of temperature sense in an area where pain sense was well preserved. One may, therefore, postulate separate pathways for pain and temperature sensibility. It would be difficult to conceive how this dissociation could be produced if there were an admixture of pain and temperature fibers within the spinothalamic tract.

In the third case, there was preservation of temperature sense with loss of pain in the presence of extramedullary compression from Pott's disease.

In this case, one may consider the possibility of increased vulnerability of the pain fibers over those for temperature sense. In a consideration of such a possibility, it must be pointed out that there are differences of opinion as to which fibers are the more vulnerable. Foerster expressed the belief that pain always suffered last, whereas other cases have been reported in which pain sensation was involved to a greater degree than temperature sense.

In view of the conflicting explanations of this type of dissociation, one might suggest further study of the problem by means of selective chordotomies, as performed by Stookey.

#### DISCUSSION

DR. A. EARL WALKER: The clinical phenomena presented are quite compatible with my concept of the arrangement of the fibers conveying the various modalities of sensation in the anterolateral tracts of the spinal cord. In all the cases presented, both pain and temperature sensibility were involved, although not necessarily in the same dermatomes. However, neither the site nor the extent, and in some of the cases not even the type, of the pathologic lesion is known, so that it is difficult to draw conclusions as to an anatomic division of pain and temperature fibers in the anterolateral tracts. In my experience with chordotomy, both modalities are always involved to some extent.

#### Cortical Activity in Cases of Post-Traumatic Epilepsy. DR. A. EARL WALKER, DR. C. MARSHALL and MR. E. N. BERESFORD.

In 39 cases of post-traumatic epilepsy the cerebral cortex was explored because of the uncontrollable epilepsy. At the time of operation electroencephalographic records were taken from the exposed cortex. In 14 cases spontaneous focal electrical alterations, such as isolated spikes, bursts of spikes or spiky waves, occurred from the cortex adjacent to, but not in, the cerebral scar. Activation of the cortical epileptogenic foci by "metrazol" or, more frequently, by a low voltage electrical stimulus induced an after-discharge, lasting from a few minutes to as long as twenty-eight minutes. No clinical concomitant occurred in 11 cases; in the rest of the cases focal sensory or motor phenomena, such as usually constituted the aura of the patient's attack, were present, and in 7 cases they progressed to a generalized seizure. Electrical stimulation of normal-appearing cortex adjacent to the focus gave no after-discharge.

The foci activated by electrical stimulation were located at approximately the site predicted by "metrazol"—activated electroencephalograms, and at the zone of spontaneous epileptic electrocorticographic alterations.

These observations indicate that certain cortical areas adjacent to cerebral scars may be excited by normally subliminal chemical or electrical stimuli, producing a local state of hypersynchrony characterized by electrical manifestations of epilepsy. That the spontaneous epileptic attacks originate from these areas lacks final demonstration, but such an interpretation seems reasonable in those instances in which the electroencephalographic attack is associated with an aura identical with that of the spontaneous seizure. Sufficient time has not elapsed to determine the

result of surgical removal of such epileptogenic foci, but to date the results have been satisfactory.

## DISCUSSION

DR. FREDERICK A. GIBBS: I had heard of the work of Dr. Marshall and Dr. Walker and now greatly appreciate hearing about it in detail. They are to be congratulated on having done an excellent job. The high quality of their recording technic could be praised, but it speaks for itself. It is a pleasure to realize that these important contributors are now back in Chicago. I was greatly disappointed, when I moved here, to discover that Dr. Walker had left.

The authors have tried various means of precipitating seizures or seizure activity. It has been rather generally supposed that almost anything will precipitate a seizure in a susceptible person. The failure of cyanide to precipitate seizures adds evidence that seizures are not easily precipitated by anoxia. The present report should provide another stone to lay on the grave of the fallacious notion that seizures are caused by such conditions as anoxia, anemia, cerebrovascular accident and functional anoxia. All recent research tends to indicate that seizure discharges are a manifestation of a specific type of pathologic physiology. In other words, seizure discharges report a highly specific type of neuronal dysfunction, and "metrazol" is a substance in a limited list of agents which initiates seizure activity.

I am aware that the long term aim of this study is to develop a better therapy of post-traumatic epilepsy. I believe that Dr. Walker has now ablated epileptogenic foci in a fair number of cases as a result of electroencephalographic studies prior to and during operation. I wonder whether he can tell us anything about the clinical results.

DR. ERIC OLDBERG: I should like to ask what were the clinical results of this operation and how many times there was a migration of the focus after such an operation was performed.

DR. A. EARL WALKER: The results of operation cannot be stated at this time because the majority of the patients were operated on within the last six or eight months. One should not pass judgment on the value of any treatment of epilepsy in which the period of observation is less than that. The longest period has been a little more than a year, and the patient has had no attacks in that time. That encourages us to continue the study.

The migration of an epileptogenous focus from one point to another occurred in approximately 6 cases. In 1 case the focus moved 6 cm. in a period of twenty-eight minutes.

We considered the most satisfactory criterion for removal of cerebral cortex a localized electroencephalographic focus which produced the clinical aura on stimulation, but we ablated the foci in about 11 cases in which we had only electroencephalographic localization.

**Electrical Stimulation of the Upper Thoracic Portion of the Sympathetic Chain in Man.** DR. A. EARL WALKER and MR. FRANK NULSON.

At the time of preganglionic or postganglionic sympathectomy for the relief of causalgia or vascular insufficiency of the upper extremity, silver clips attached to enameled copper wires were placed on the sympathetic chain between the second and the third thoracic ganglion. The wires were led out through the incision in the skin and included in the sterile dressing.

Stimulation of the sympathetic chain was carried out from forty-eight hours to eight days after operation, in many cases a series of stimulations being made at one to three day intervals. A careful record was kept of the sensations noted by the

patient and of any objective changes in the extremity, particular attention being paid to the time relationship. When the cutaneous sutures were removed, the wires and clips could be withdrawn readily. No untoward reactions resulted from the procedure.

In 4 cases of the causalgic syndrome and in 6 cases of pure vascular insufficiency preganglionic section was the procedure. In the other 2 cases, of vascular insufficiency without pain, postganglionic section was done.

As might be expected, the majority of *bona fide* sensations were confined to the local area in the back or to the distribution of the second and third intercostal nerves. However, pain in both the hand and the arm occurred on stimulation in 3 of the 10 cases of preganglionic sympathectomy; interestingly, causalgia was present in all 3. In these cases a characteristic and reproducible pattern of response was shown.

A delay of four to twenty seconds was present between the stimulus and the patient's experience of discomfort. The discomfort was variously described as a tingling, burning or pricking sensation in the fingers, hand or arm. It might be localized to one surface of the hand or to an individual finger—usually the little finger. It gradually increased in severity until a maximum was reached in fifteen to thirty seconds. Even though the stimulus was continued, the discomfort slowly decreased and disappeared within fifteen to thirty seconds after the peak. In 2 cases the subjective complaints were closely paralleled in time by a visible pilomotor response over the entire arm and shoulder. This appeared a few seconds before discomfort was noted and faded away simultaneously with the pain. There was often a low grade aching in the arm or hand for as long as twenty-four hours after stimulation.

The type of response to stimulation was quite different in the 2 cases of postganglionic division of the sympathetic chain. Localized pain in the back and chest only was experienced immediately on application of the stimulus. The absence of pain in the arm was not unexpected for the efferent connections of the sympathetic trunk were sectioned. The local pain might be explained on the basis of stimulation of visceral afferent fibers or of neighboring intercostal nerves.

In patients with causalgia there appeared to be a relation between the peripheral effects of sympathetic activity and the production of pain.

DR. A. EARL WALKER: There is clinical evidence to favor the belief that there is a relation of the scar tissue to causalgia. In some cases of causalgia with lesions of the tibial nerve, it was found that sympathectomy of the portion of the leg to which the pain was referred did not relieve the pain, but if the sympathectomy was carried higher, so that the actual site of the lesion in the tibial nerve was sympathectomized, complete relief occurred. This suggests the possibility that the sympathetic fibers in the scar at the site of injury were responsible for the disturbances. There is also good physiologic evidence that there is a cross firing at the site of the scar. Action potential studies of the afferent root have shown that in an injured peripheral nerve there is a reflux of stimuli, which are applied to the afferent portion of the nerve, a condition likewise favoring this situation.

The pain in the elbow may best be explained by local implication of the second intercostal nerve. We have had occasion to stimulate a patient with Raynaud's disease. She complained of pain in two areas, one in the chest and one in the elbow, but never in the hand or in the forearm. In my opinion, the best explanation of that distribution was spread to adjacent intercostal nerves.

## Book Reviews

**Sexual Behavior in the Human Male.** By A. C. Kinsey, Sc.D.; W. B. Pomeroy, and C. E. Martin. Price, \$6.50. Pp. 804. Philadelphia: W. B. Saunders Company, 1948.

This book has already evoked wide discussion in lay and professional groups. One hears that the book clubs eagerly sought after it. A columnist claims it is more thoroughly known to the general public than the Marshall plan. Indeed, it is now fourth on the best-seller lists. Fact and rumor attest to its impact on the public.

The question arises: Is its wide circulation a contribution to the public weal? This reviewer believes it is.

Kinsey and his associates have attempted a laudatory investigation of the sex habits of the American male. Previously such information as was available was based on worn, but traditionally accepted, fact and fancy, inadequate studies and so-called intuitive knowledge. With his experience as a biologist as a discipline, Kinsey has striven to make his study statistically accurate within obvious bounds. Carping critics have rushed to attack his analyses of data. It is patently impossible to control completely such a statistical problem. Kinsey is the first to warn the reader against the validity of many of his assumptions and deductions. He stresses the need for a larger and more exhaustive sampling of the population.

The conclusions meet the test of clinical experience. Few sociologists and clinicians would quarrel with the authors' summings up. For the professional worker, the Kinsey report will serve as a vast fund of reference data. For the psychiatrist, it will prove important background in the analysis of individual problems. It may often serve to replace or bolster previous impressions of the range of "normal" behavior in the human male.

It may also in certain instances demonstrate that eccentricities of behavior may originate in group background rather than in purely individual experience.

Certainly, the entire subject is on firmer ground when treated in the Kinsey manner than in its previous state. If the book did nothing more than point up the need for further exhaustive studies, it would serve a most useful function. Kinsey and his colleagues deserve greater credit, however. They have made a fundamental contribution to the better understanding of human behavior.

**Psychotherapy in Child Guidance.** Gordon Hamilton. Price, \$4. Pp. 340. New York: Columbia University Press, 1947.

This book stems from a study of child guidance at the Jewish Board of Guardians in New York undertaken several years ago by Gordon Hamilton, professor of social work, New York School of Social Work. Direct therapy with children has been conducted by social workers at the Jewish Board of Guardians for several years now, and Miss Hamilton attempts to describe the program's orientation and to show that psychotherapy may be "appropriately practiced in a social work rather than a medical setting." The book is for the most part a textbook of psychoanalytic theory with fragmentary case material. There is no

discussion of such fundamental issues as duration of therapy, results or the relative roles of concomitant treatment of child and parent. It is unfortunate that data on these subjects are omitted; without them it is impossible to assess the function or value of any treatment program.

The writing throughout the book is direct and lucid, although the content is at times oversimplified. There is excellent treatment of the theoretic differentiation of primary conduct disorders and neurotic disorders and of the concept of preoedipal and oedipal types. This differentiation receives major stress in the study. There is discussion of the problems of transference, countertransference, resistance and the dynamics of change. The material on "therapeutic attitude" is provocative, emphasizing an almost total permissiveness. In practice, inordinate stress on acceptance and permissiveness proves insupportable for many children, tends to diminish, rather than increase, rapport and is conducive to therapy being prolonged or losing direction.

In this guidance setting the psychiatrist acts as consultant to the case worker, but the extent of his participation is not indicated; Miss Hamilton's references to this issue suggest that it is limited. There is no question that nonmedical therapists must be trained to meet the present needs for treatment. It is astonishing, however, to find Dr. Ackerman stating in his foreword that the case worker, rather than the psychiatrist, should assume the role of therapist because the psychiatrist is not equipped to deal with the whole range of the child's problem, presumably because of his lack of knowledge of "social patterns." Such rationalization should be unnecessary to justify therapy by adequately trained case workers. The integration of disciplines obtaining in the best child guidance clinics today certainly brings to patients the full benefit of a knowledge of "social patterns." There may still be some advantage to the patient in the therapist's full training in clinical medicine, psychiatry and hospital and clinic practice! Dr. Ackerman's statement is particularly paradoxical in view of what follows in Miss Hamilton's text. The approach described is for the most part unifocal, mechanistic and often essentially theoretic. Psychologic mechanisms are redefined with little regard to either growth processes or cultural pressures.

The practice of direct psychotherapy by social workers is a major trend in psychiatric treatment today and calls for general consideration and evaluation. Miss Hamilton and the Jewish Board of Guardians are to be congratulated on providing this provocative and challenging study. The book deserves a wide reading and furnishes material on a particular psychoanalytic orientation that should prove stimulating reading for all therapists.

**Training in Clinical Psychology.** Transactions of the First Conference, March 27-28, 1947. Price \$1.50. Pp. 87. New York: The Josiah Macy Jr. Foundation, 1947.

As a result of the increased awareness on the part of the public of the need for psychiatric and psychologic care, the spotlight has been turned increasingly on clinical psychology by those active in this field, as well as by those in allied professions. Among the major concerns of these persons is the nature of the training that shall be required for the making of a good clinical psychologist, and this further involves the question, "What is a clinical psychologist, and in what areas shall he operate?" A two day conference was held under the auspices of the Josiah Macy Jr. Foundation in an effort to get an exchange of ideas on this matter and so to help construct a working program for training in clinical psychology. The meeting was attended by psychiatrists, psychoanalysts, psychologists and psychiatric social workers.

The papers read at these round table sessions are reported in this pamphlet, along with the discussion and comment they provoked. This review is, therefore, not actually a book review but an evaluation of the conference itself and the ideas arising in it.

The plan of this conference was a most timely one, and the way in which it was executed cannot be too highly commended. It was apparent from the statements made by the various participants at the conference that they were attempting to meet the problem squarely and vigorously, without being hampered by outworn concepts or awed by vested interests, either academic or professional. The need for the development of a new approach in training the psychologist who is to work with the emotionally disturbed and mentally ill patient was clearly recognized by all, and there was no hesitation in brushing aside established tradition when this seemed to interfere with the desired ends. Thus, Harrower stated that "by no stretch of the imagination can it be argued, or by wishful thinking asserted, that there is anything in the regular Ph.D. in academic psychology *per se* which remotely equips him [the psychologist] to do therapeutic work"; or, again, "a psychologist may be considered clinical when he has lost his experimental rigidity sufficiently to realize that . . . the rules for administering a test are not ends in themselves."

Existing lacks in psychologic training, especially in regard to the acquisition of an optimally professional attitude toward the client or patient, was stressed by Miller. He called attention to the differences in training offered by medical schools and academic graduate schools. In the latter, emphasis is on research, the writing of doctoral dissertations and written and oral examinations. In medical training, much opportunity is provided for working with the patient directly. Along with this, the medical student is inculcated with a sense of his responsibility for the welfare of those with whom he comes in contact. He also has had an opportunity to see sick people in action, not in a rarefied laboratory setup. Miller expressed the belief that the clinical psychologist throughout his training should have as much opportunity as possible for contact with patients, rather than that such contacts be restricted to one special course.

The question of research in clinical psychology was also discussed. The psychologic clinician, by virtue of his special equipment and the instruments he uses, can throw much light on personality dynamics, can objectively evaluate the efficiency of various types of treatment and can offer further refinement in questions of diagnosis. These research functions of the clinical psychologist are all-important ones.

The all pressing question of therapy was given much consideration. The enormousness of the community needs and the paucity of available therapists were stressed by Kubie, who outlined a program for the selection and training of psychologists to function as therapists in filling at least part of this gap. On the other hand, Binger argued that the more therapists are available, the more services would be demanded; and he therefore expressed the belief that an understanding of neurotic illness, so that preventive measures might be adopted, was more important at this point.

The training of the psychiatric social worker also came into review. Here, again, the discrepancy between the opportunities for field work during training as provided by this profession and those afforded in psychology is most striking.

In general, there was recognition that increased opportunities and special courses geared for the special needs of clinical psychologists are slowly appearing in various universities. Different discussants held different points of view as to where such training should take place. The possibility of setting up a special

school for training in clinical psychology was mentioned; a modified program carried out in the medical school was suggested, as was radical reorganization of the existing academic programs. None of the members of the conference felt they were prepared to offer more than tentative suggestions because of the present lack of reliable information regarding the training of those in clinical practice and the present changing attitudes of the various institutions of learning toward the profession of clinical psychology.

That the question is an all-important and pressing one was evident from the general lack of satisfaction with the existing state of affairs in regard to clinical psychology among those present at the conference. Similarly these workers recognized the urgency for doing something about the matter. Their lack of agreement as to what should be done reflects the present cross currents in the field, the general lack of uniformity in training and an inability even to define what the clinical psychologist is and what he can and should do. Continued sessions such as this initial one are therefore urgently needed in order that a program may be set up and recommended to various training institutes or, what seems even better, efforts directed toward the establishment of a separate school for training in clinical psychology.

**Problems of Early Infancy.** Edited by Milton J. E. Senn., M.D. Price, 75 cents. Pp. 70. New York: Josiah Macy Jr. Foundation, 1947.

The first conference on problems of early infancy, sponsored by the Josiah Macy Jr. Foundation, was held in New York in March 1947. The transactions have been published in a small, inexpensive volume, edited by Milton J. E. Senn. Discussions by some twenty-five authorities, representing many disciplines, are reported. The major areas considered are anticipatory guidance for prospective parents, mother-child relations, breast feeding, self-demand schedules and rooming-in projects for mother and child.

Senn points out the importance of anticipatory guidance in preparation for parenthood. In the discussion that follows, the practical difficulties are stressed, especially limitations in personnel and time. It is assumed that this guidance will be on an individual level; it would seem that group discussion or group therapy is particularly appropriate in this area, with specific advantages in terms of interaction between participants.

Anthropologic data on mother-child relations and breast feeding are given by Maloney and Mead. Olmsted cites interesting statistics from the Grace-New Haven Community Hospital on the reasons for mothers' discontinuing nursing: insufficiency of milk, 30 per cent; no desire to nurse, 25 per cent; poor health or poor home situation, 21 per cent; baby's admission to hospital, 12 per cent, and complications of mastitis, 12 per cent. Walser points out the essential problem in this area, stating that he feels "very firmly convinced that we need actual teaching facts to present to certain of our expectant mothers, which at present we do not have. We must be able to say why breast-fed babies are better than bottle-fed babies."

Perhaps the most important section of this report deals with experiences with rooming-in projects in New Haven (Olmsted; Jackson), New York (Fries) and Detroit (Montgomery). Advantages in terms of fostering positive feelings of the mother toward the infant, increasing gratifications for the infant and providing the opportunity for early relationship with the father are stressed. On the other hand, Escalona points out possible contraindications; namely, the anxious mother, having almost complete responsibility for the infant, may have difficulty in meeting

his needs, and he may be exposed to severe maternal tension or disrupting overstimulation. While the value of the rooming-in projects emerges clearly, it would appear that the establishment of criteria for the selection of mothers is indicated.

Many conflicting and divergent opinions are expressed in this volume, and the point of view taken by Butler is valid; he states: "The development and elaboration of theory concerning child rearing and techniques for synchronizing education with the rate of rhythm of growth are urgently needed; testing continually the validity of theories by appraising objectively the results obtained by their application is equally important."

**The Metabolic Brain Diseases and Their Treatment.** By G. Tayleur Stockings, M.B., B.S., D.P.M. Price, \$4.50. Pp. 262 Baltimore: Williams and Wilkins Company, 1947.

This is a systematic presentation of the theory that the so-called functional psychoses are "metabolic encephalopathies." Under metabolic encephalopathies the author recognizes two main clinical subdivisions: (a) dysoxic encephalopathy, or dysoxia, and (b) dysglycic encephalopathy, or "dysglycia." The first group includes affective states; certain forms of paranoid, catatonic and mixed depressive-schizophrenic conditions; some forms of obsessional states, and conditions characterized by depersonalization. These conditions are due to disorders of the oxidative mechanisms and respond only to anoxic, i.e., convulsive, therapy. The second group ("dysglycia") comprises hebephrenia, "simple manic" conditions, paraphrenia and paranoia and is due to disorders of the glycolytic mechanisms. Such conditions respond only to hypoglycemic therapy, i.e., insulin shock.

"Metabolic encephalopathy is a curable and even preventable condition—provided diagnosis be early and treatment thorough and adequate . . . Our knowledge of cerebral physiology, the pathology of metabolic disorders, and the mechanism of neurometabolic therapy is as yet only in its infancy, and the immediate future holds out limitless hopes and possibilities for research along these lines."

This book should be read by all psychiatrists who are interested in physiologic methods in psychiatry. It is an admixture of fact, theory and speculation. Its value is perhaps somewhat impaired by dogmatic assertion.

**A Textbook of Clinical Neurology**, with an Introduction to the History of Neurology. Sixth Edition. By Israel S. Wechsler, M.D., Clinical Professor of Neurology, Columbia University College of Physicians and Surgeons. Price, \$8.50. Pp. 829, with illustrations. Philadelphia: W. B. Saunders Company, 1947.

Since its previous edition, this standard text of clinical neurology shows few major changes. The author states that the new edition serves equally to reaffirm to the medical profession neurology as a discipline and to introduce the newer knowledge. Because it is so well known, comments will be confined to the revisions. The format and general plan remain unchanged. David Wechsler has renamed his section "Psychological Diagnosis" and has rewritten it from the broader point of view of general function of the brain and specific dysfunctions in organic cerebral disease. He points out the usefulness of psychometry to the neurologist: (a) in determining degrees in mental retardation, (b) in clinical and differential diagnosis, (c) in rehabilitation and reeducation by determining the patient's actual and potential abilities and (d) in "compensation cases." The battery of psychologic tests discussed is expanded, the mental mechanisms resulting from frontal lobotomy are evaluated. Descriptions of several syndromes have been added: porphyria polyneuropathy, toxoplasmic encephalomyelitis, congenital muscular

torticollis, hemangioma of the vertebra and sleep paralysis. The syndrome of lateral sclerosis is now considered by the author a primary condition if, over a sufficiently long period of observation, no change occurs in the patient's state which would indicate that another condition has been present, though slowly evolving. The section on sciatica has also been revised. The newer concept of amyotonia congenita (Oppenheim) as a defect of the entire motor system, from Betz cell to muscle, goes without mention. Treatments have been brought up to date. Neostigmine and vitamin E are advised for amyotrophic lateral sclerosis, though in general they have had little effect in influencing the course of the disease. The use of trimethadione ("triodine") in management of petit mal epilepsy is noted. Neostigmine and curare are not mentioned with reference to the treatment of spastic states, although the use of the latter in cases of acute anterior poliomyelitis is suggested, as it seems to affect the paralysis favorably. Penicillin in the treatment of purulent infections of the nervous system is dispensed with in a single sentence, "Penicillin is more effective than the sulfa drugs." The dosage, intrathecal use and dangers of the drug are omitted. Its use with the various forms of neurosyphilis is given but slightly more attention. This is somewhat surprising in view of the large role this antibiotic is playing in the cure of these conditions. Perhaps the author considers that detail is unnecessary because of the common and widespread application of the drug. Equally as startling is the complete omission of streptomycin therapy of tuberculosis. Other less significant changes have been made throughout the text. The references have been rearranged and brought up to date in many instances. A number of new illustrations have been added, and some old ones have been discarded. Though the omissions and brevity of the references, as noted here, do not seriously subtract from the usefulness of the book for the seasoned practitioner, who has many sources of information, they may be important to the student or the intern confronted with the treatment of these conditions. The value of this book still lies in its lucid, succinct, accurate descriptions of neurologic diseases, with its stress on their functional anatomic basis, and in its all-inclusiveness.

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